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NEURONAL ADAPTIVE MECHANISMS UNDERLYING  
INTELLIGENT INFORMATION PROCESSING

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specific stimulus combination, the code depending on the order and i specific input signal. Research indicates that the pattern of cortical neuronal activity produced by hypothalamic stimulation predicts loci of hypothalamic stimulation that, when, stimulated, will succeed in accelerating learning. Present studies are directed toward establishment of whether the hypothalamic stimulation responsible for acceleration of learning is punishing or rewarding. This may, however, be of less consequence in understanding what is going on than would specifying the coded molecular interactions that occur between the chemical(s) released by hypothalamic stimulation and other chemicals capable of modifying the transfer properties of the nerve cell. It is these interactions that are thought to be primary in controlling the potentiation of learning.

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\*The experiments reported herein were conducted according to the principles described in Guide for the Care and Use of Laboratory Animals DHEW Publication (NIH) 78-23.

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## I. SUMMARY

Acceleration of the rate of learning of a conditioned facial movement was accomplished by adding electrical stimulation of the hypothalamic region of the brain to presentations of conventional conditioned and unconditioned stimuli, confirming earlier Soviet observations of a comparable effect of such stimulation.

The learning that resulted was both associative and discriminative. That is, learning was induced by a specific stimulus combination, the code depending on the order and interval of presentations of two different stimuli. The learned response was then elicitable by a specific input signal.

Our research indicates that the pattern of cortical neuronal activity produced by hypothalamic stimulation predicts loci of hypothalamic stimulation that, when stimulated, will succeed in accelerating learning.

Part of the acceleration of learning the motor response may derive from recruitment of a new performance pathway - reflected in a longer transmission latency for movement production. If so, one would like to know how the system picks the "right" pathway to give both acceleration and the "appropriate" learned movement.

Present studies are directed toward establishment of whether the hypothalamic stimulation responsible for acceleration of learning is punishing or rewarding. This may, however, be of less consequence in understanding what is going on than would specifying the coded molecular interactions that occur between the chemical(s) released by hypothalamic stimulation and other chemicals capable of modifying the transfer properties of the nerve cell. It is these interactions that are thought to be primary in controlling the potentiation of learning.

What is particularly interesting to us is the indication that purposefully complex, "lock and key" molecular cascades exist at the level of single nerve cells to permit "successful" adaptations to occur. "Successful" adaptations are defined as: (a) producing the desired alteration of response to the appropriate input, (b) enduring over time, (c) not interfering with other adaptations occurring for other purposes in the same cell, and (d) not interfering with the main - throughput - message transfer property of the nerve cell. The result of these adaptations is to support the operation of a self-organizing information processing system with a high success: error ratio and excellent survivability in the face of substantial environmental change.

The nerve network and elements that were studied reflect a much different design from that found in single elements of most artificial information processing devices. Nonetheless, the design seems understandable in terms of conventional information processing theory and in terms of conventional systems analysis approaches. (For a brief summary of the latter see the enclosed Appendix excerpted from a recent book of mine.)

Some of the complexities of these nerve cell adaptive operations are exemplified by:

(a) A conductance decrease IPSP that we have found after PT stimulation (this mechanism for altering neural excitability works in just the opposite way from classical conductance increase mechanisms of PSP generation),

(b) The fact that both a strong depolarization signal and the availability of a calcium-activated protein kinase or analogously activated post synaptic modulatory chemicals may be needed to change the membrane response (to acetylcholine or cyclic GMP) from a transient change to a persistent one.

We think that we are now catching "glimpses" of some surprisingly sophisticated ways in which cortical neurons adapt to support a whole range of newly learned tasks, accomplishing the task at hand while maintaining the potential for accomplishing others.

## II. STATEMENT OF WORK

The human brain is the most powerful adaptive network known to man. It is responsible for human intelligence with operations involving automated image recognition, speech, decision making and complex motor functions. The same functions are the goal of artificial intelligence operations, robotics and the like. Attempts to design machines to perform these functions successfully would benefit from an understanding of how the brain has succeeded in doing so.

Both brain and machine depend on component operations. There is reason to believe that systems supporting complex goal-seeking adaptive behavior are best constructed out of goal-seeking adaptive components. Limited understanding of how such components work has prevented their incorporation into present artificial intelligence systems.

In the brain the basic component is the neuron. Recent studies indicate that single cortical neurons adapt in such a way as to support adaptive mammalian behavior. Post-synaptically, adaptation is reflected at the cellular level by a change in neural excitability to injected current. We have focussed our studies on analysis of this type of adaptation.

Twelve publications have resulted from the research in this period; see list of publications - Part IV. The ultimate goal of the research is to provide a foundation for the design of improved adaptive network architectures.

### III. COMPREHENSIVE PROGRESS REPORT - STATUS OF RESEARCH

#### A. April 1981 to present

1. The effects of US presentations on rates of discharge and excitability to weak extracellular current were determined in single units of the motor cortex (Brons, Woody and Allon, J. Neurophysiol., 1982). The excitability to weak (nA) extracellular electrical stimulation was measured among single neurons of the pericruciate cortex of awake cats as a function of behavioral state. Levels of neuronal excitability were compared 1) after classical conditioning of a facial movement, 2) during extinction of the conditioned response, and 3) during unpaired presentations of conditioned and unconditioned stimuli (CS and US).

Neurons projective to facial muscles via polysynaptic corticofugal pathways showed decreased levels of excitability to weak extracellular stimulation following conditioning with forward pairing of the CS and US, extinction with backward pairing of the stimuli, and presentations of the US alone. These changes in excitability were attributable solely to the effects of US presentation and were not distinguishably different during either conditioning or extinction of the behavioral response. Small decreases in rates of spontaneous firing were found to accompany the decreases in neural excitability.

The data support the conclusions that significant nonassociative changes in neural excitability occur during conditioning and extinction due to presentations of the unconditioned stimulus. These changes support latent inhibition, behaviorally, and the mechanism of these changes is different from that of changes in postsynaptic excitability found, after conditioning, by intracellular stimulation of similar cortical neurons (Woody, Fed. Proc., 1982). The increased excitability to intracellular currents facilitates performance of the specific type of motor response that is acquired and is also latent, awaiting a command signal that will cause the response to be initiated.

2. The rapidity of acquisition of conditioned motor responses was determined after adding hypothalamic stimulation to click CS and glabella tap US. Our analyses show a two order-of-magnitude acceleration of the rate of acquisition of a blink response over that achieved by pairing the same CS and US without hypothalamic stimulation (Kim, Woody and Berthier, J. Neurophysiol., 1983). Changes in the patterns of activity of single units of the motor cortex are isomorphic with the development of the conditioned response (Woody, Kim and Berthier, J. Neurophysiol., 1983).

Additional findings were obtained following completion of the following computer programs.

#### Computer Program

The program consists of three functional units: stimulus presentation and data collection, histogram generation and display, and behavioral analysis and data storage. Conditioned (CS), unconditioned (US), hypothalamic (HS), and discriminative (DS) stimuli are presented in a timed sequence for ten second trials of adaptation, conditioning, extinction, or delayed HS paradigms. Timing of stimuli can be generated spontaneously for on line experiments or



synchronized to an analog tape pulse for analysis of prerecorded data. During each trial, five seconds of EMG data encompassing all stimuli are sampled at 2 ms intervals from the left and right orbicularis oculi and levator oris. Eight histograms are generated from the data and displayed four each on Mime 100 and VT105 video terminals. The histograms are averages of three trials and are normalized to the tallest bin. The Mime 100 histograms are 400 ms displays encompassing the CS-US period for each EMG. The VT105 histograms can be dynamically modified by keyboard codes which can center histograms around any stimuli for any EMG and display from 100 to 1600 ms of data.

The computer detects conditioned EMG responses using the criteria that 3 consecutive samples in the current trial plus 1 of the 2 previous trials plus the average of those 3 trials must exceed 5 standard deviations above the mean of spontaneous activity sampled for 400 ms before the CS. The response must be detected between 100 ms after the CS and 20 ms before the US. If a response based on these criteria is found, the three trials are individually stored on disc while no response results in three trials being averaged before disc storage.

### Results

The results of training cats with click CS, tap US, hypothalamic stimulation (HS), and an added hiss DS are shown in Figure 1. They indicate that, with this paradigm, discriminative responses to the CS are acquired within 9 trials. The rate of acquisition is two orders of magnitude faster than when HS is omitted and permits intracellular recording from cortical neurons while learning takes place. The latencies of the CRs range between 100 and 300 ms.

Additional effects on conditioning of adding hypothalamic stimulation (HS) to classical application of CS (click) and US (glabella tap) have also been examined:

- a. Videotapes were made comparing learning in animals given stimulation at effective hypothalamic loci with failure to learn in animals given stimulation at ineffective hypothalamic loci. Figure 2 shows some effective and ineffective loci (Kim, Woody and Berthier, *J. Neurophysiol.*, 1983).
- b. Patterns of cortical unit response to hypothalamic stimulation may be predictive of an effective locus of hypothalamic stimulation for producing enhanced rate of learning. Patterns of activity such as that shown in Figure 3 have been seen with effective hypothalamic stimulation (Woody, Kim, and Berthier, *J. Neurophysiol.*, 1983).

3. Pilot studies are underway to determine if the hypothalamic stimulation that leads to accelerated learning of a conditioned movement is rewarding or aversive (Berthier et al, *Soc. Neurosci. Abstr.*, 1982). Preliminary findings suggest that either a mildly aversive or a rewarding stimulus may produce accelerated learning. Further studies are underway to obtain further information on this question.

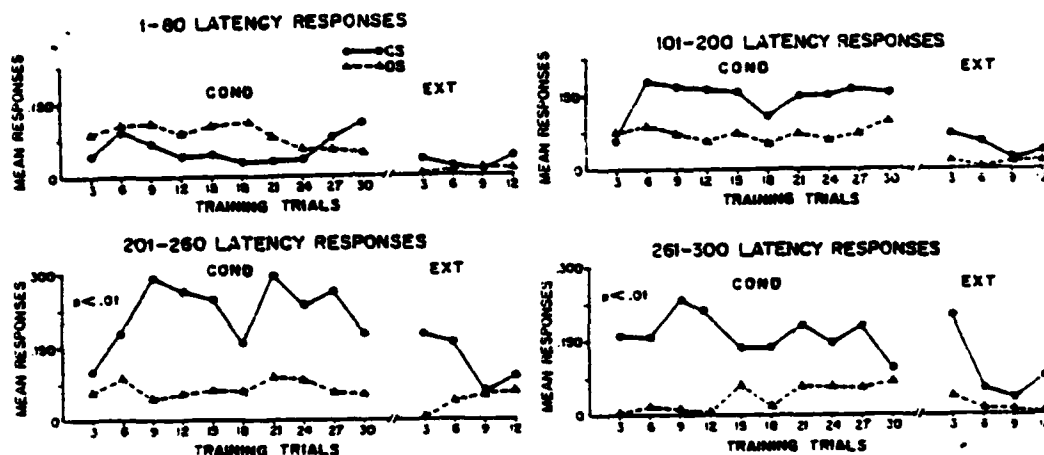
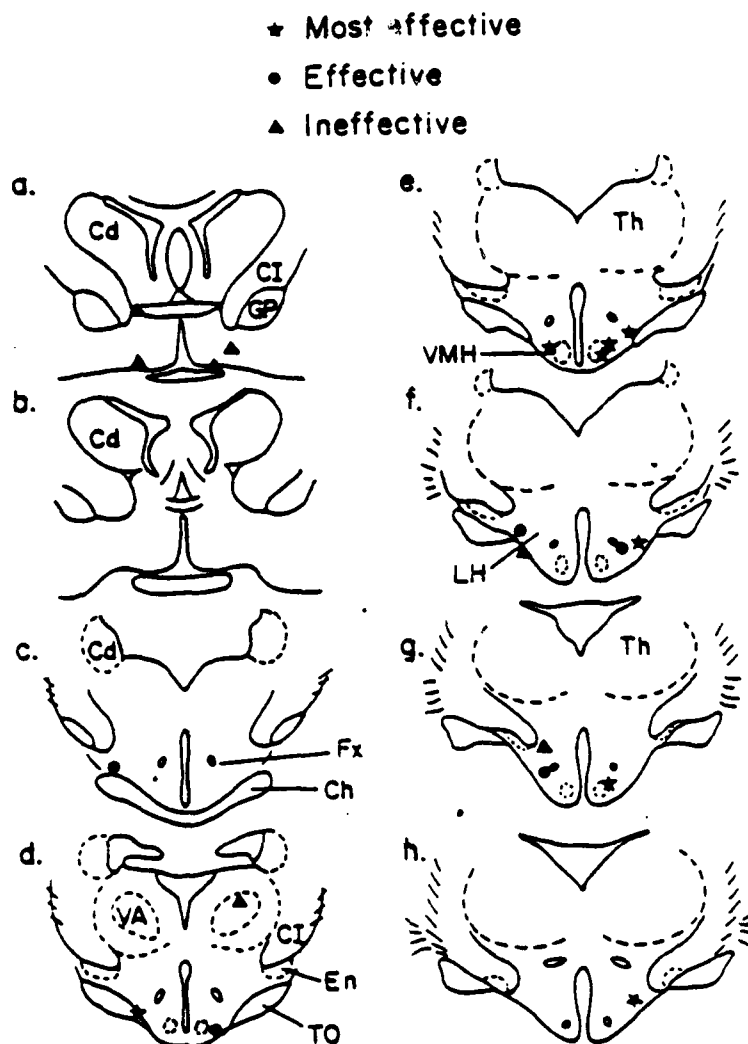


Figure 1. Rapidity of Conditioning and Latency of CR's

Development of EMG responses of different latencies to CS (Solid line) or DS (Dashed line) in 8 cats during conditioning. Responses were defined as EMG responses of greater than 5 sd above the pre-CS (spontaneous) mean. During training, CRs increased with trials reaching asymptote (74% CRs) within 9 trials. Responses were classified into four windows (0-80 ms, 101-200 ms, 201-260 ms, 261-300 ms; top to bottom, respectively). Cats made more responses to the CS than DS when responses of greater than 101 ms were analyzed. During extinction cats made more responses to the CS than to the DS, but by the ninth trial of extinction there was little responding to either the CS or DS.



**Figure 2. Loci of Brain Stimulation**

Filled stars represent hypothalamic sites, stimulation of which produced rapid acquisition of discriminative eye-blink CRs at over 90% performance level. The sites of stimulation that resulted in discriminative CRs being performed less consistently are represented by filled circles. Behaviorally ineffective sites of stimulation are indicated by filled triangles.

Abbreviations: Cd, caudate nucleus; Ch, optic chiasm; CI, internal capsule; Fx, fornix; GP, globus pallidus; LH, lateral hypothalamus; Th, thalamus; TO, optic tract; VMH, ventromedial hypothalamic nucleus.

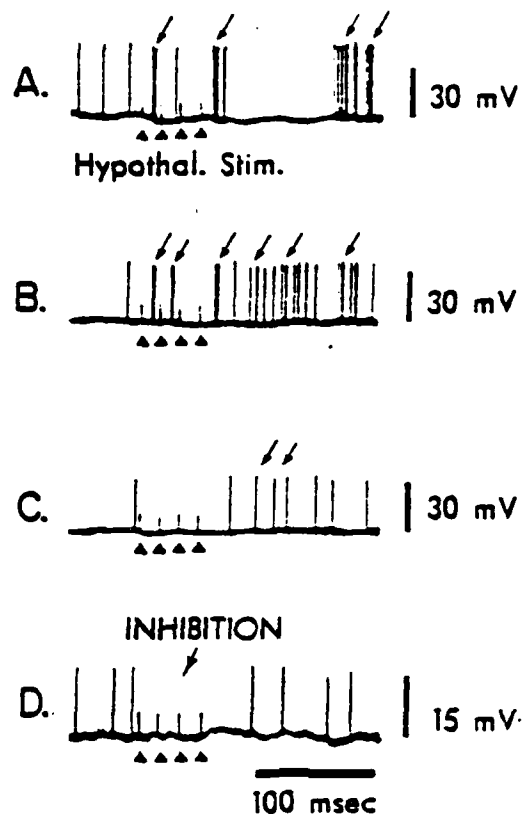


Figure 3:

Effects of hypothalamic stimulation on single unit activity recorded from different cells in the coronal-pericruciate cortex. Examples of different cortical unit responses to the first train of stimulation are shown. The triangles appearing below each tracing indicate the train of four brief (0.1 msec duration) stimulation pulses. Small downward arrows point to the spikes.

Hypothalamic stimulation resulted in:

- A. Early excitation followed by inhibition.
- B. Early and late excitation
- C. Late excitation
- D. Inhibition

Calibrations are as indicated.

4. Effects on cortical neurons of intracellular application of cyclic AMP (cAMP) have been investigated. cAMP was applied by pressure microinjection (0.1 mM solution in 4% HRP injected at 60-80 psi for 1-5 seconds). The following effects were seen in HRP injected cells: a) increases followed by decreases in firing rate, b) hyperpolarization, c) small decreases in membrane resistance, d) small decreases in excitability to intracellularly injected current. Pyramidal cells of layer V were among those showing these responses. The results indicate that excitability and membrane resistance are decreased by intracellular cyclic AMP. Control studies with intracellular applications of 5' AMP (an inactive, metabolized form of cyclic AMP) did not show these effects. The differences between experimental and control groups were statistically significant.

5. Effects of PT stimulation on PSP production were studied in intracellular recordings from 62 cells of the motor cortex of awake cats (Bindman, Woody, et al, Soc. Neurosci. Abstr., 1982). Of these cells, 10 showed an IPSP that decreased with hyperpolarization and, in 5 of the 10 cells, the IPSP was reversed with additional hyperpolarizing current. In 9 of the cells, it was possible to measure a decrease in resistance at the time of the IPSP. This IPSP has been recognized previously by other investigators and is thought to reflect an increase in chloride conductance. In 30 of the remaining cells, a quite different IPSP was found during the same 35-120 msec period following PT stimulation. In each of these cells, the IPSP increased in size with the application of hyperpolarizing current and could not be reversed with hyperpolarization (see Fig. 4). With depolarizing current the IPSP decreased in size. The resistance was measured at the time of the IPSP by comparing the magnitude of a continuously repeated (20 ms on, 20 msec off) bridge pulse during the IPSP with that prior to the PT shock that elicited the IPSP. An increased resistance was found to accompany the IPSP. Conductance decrease IPSPs were seen in these cells irrespective of whether antidromic spikes were produced by PT stimulation. Conductance decrease IPSPs have been reported previously (Siggins et al, 1971; Engberg and Marshall, 1971; Smith and Weight, 1977), but not in neurons of the motor cortex. [PT stimulation is an effective US in producing conditioned behavior [O'Brien et al., 1977].]

6. Injections of calcium ions and HRP were made intracellularly in neurons of the motor cortex of awake, unparalyzed cats. Pressure injection was used to avoid voltage dependent calcium flux that could arise from iontophoretic application. Twelve cells with resting potentials averaging 49mV were injected with 4% HRP in  $10^{-3}$  M  $\text{CaCl}_2$ . Twenty-nine cells injected with HRP without additional calcium had resting potentials averaging 47mV. Injections with calcium produced an increase in conductance measured by the differential spike height method that was usually sustained over the course of 3 minutes. Injections of HRP alone produced no change or significantly smaller conductance increases. HRP solutions were found to contain as much as  $10^{-4}$  M free calcium ions. Cells responding to calcium with a conductance increase were identified as pyramidal cells of layers II, III and V (Wallis et al., Soc. Neurosci. Abstr., 1982).

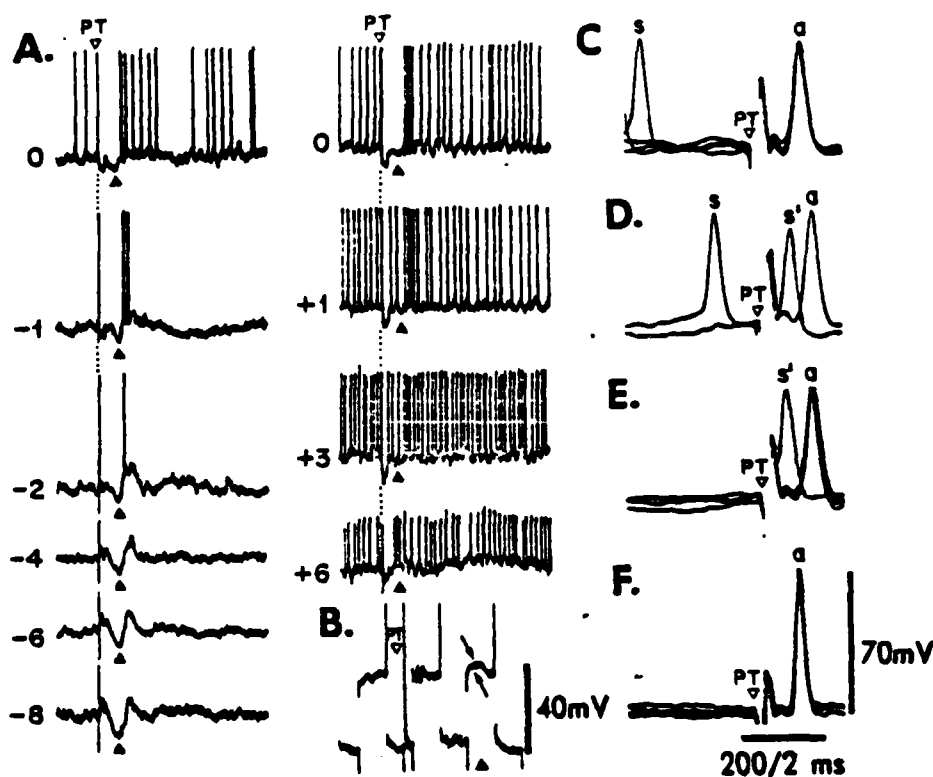


Figure 4. An antidromically activated neuron of the motor cortex with an IPSP (arrow) that increased with hyperpolarizing current. A: Effects on the IPSP of applying both negative and positive steady current (values in nA as shown). An increase in the rate of spike discharge and a reduction in spike amplitude accompanied the application of steady depolarizing current. The times of delivery of the single PT shocks are as indicated. B: Applications of the recurrent 1nA depolarizing pulse used to measure resistance in this cell. The resistance is increased at the time of appearance of the IPSP (arrows). C-F: Antidromic spikes (a) elicited by PT stimulation. Note invariant latency of occurrence and collision with spontaneously occurring spikes. Spontaneously generated spikes (S') that occur during conduction of the antidromic spike block the appearance of the antidromic spikes as shown in D and E; other spontaneous spikes (S) do not. Application of steady hyperpolarizing current (-8 nA) in F results in an increase in the size of the antidromic spike. (The tops of the spikes are cut off in comparable portions of A.) The voltage calibration in F applies to all records except B, for which a separate calibration is given. The time calibrations are for A and C-F respectively; the depolarizing pulses in B are of 15 ms duration.

7. Research on control mechanisms supporting neural adaptation was conducted collaboratively with Dr. D. Alkon at the Woods Hole Marine Biological Laboratory. Attempts were made to detect changes in membrane properties controlling the development of excitability increases found after conditioning. Cat preparations were supplied by Dr. Woody. Modifications of our electrodes introduced by Dr. Alkon facilitated measurement of these changes.

The effects on membrane resistance of injecting calcium-calmodulin dependent protein kinase intracellularly in units of the motor cortex were studied in awake cats. Some preliminary results are shown below in Figure 5.

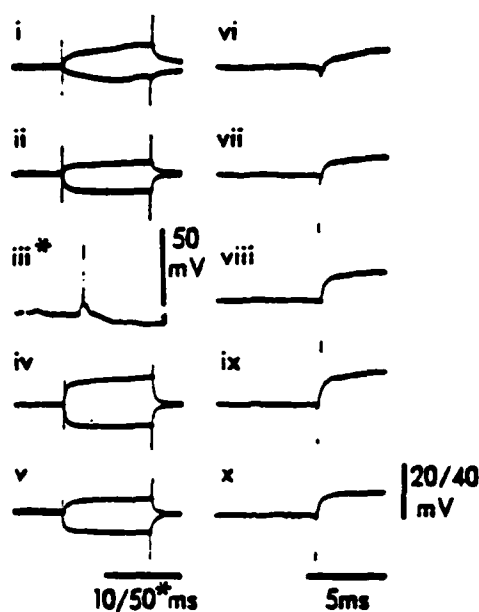


Figure 5. Results of intracellular injection of calcium-calmodulin dependent protein kinase and application of depolarizing current. Resistance (i) - before protein kinase injection, (ii) - after protein kinase injection; (iii) - spike recorded during hyperpolarizing iontophoresis of protein kinase; resistance (iv) - immediately after depolarization subsequent to protein kinase injection, (v) - ten seconds after cessation of depolarization; (vi - x) - faster, amplified sweeps showing bridge balance at periods corresponding to those in the traces to the left, except for (viii) which shows the bridge rebalanced prior to the 30 sec period of depolarization. Control studies performed with electrodes filled with KCl without protein kinase failed to show resistance increases. Calibrations are as indicated below and to the right of each portion of the figure. The voltage calibration applies to i, ii, iv, v and vi-x, respectively.

It appears that some of the same control mechanisms responsible for elaboration of associatively induced behavioral changes in Hermisenda are

operative in neurons of the cat motor cortex that support the performance of learned motor tasks.

What is interesting about these mechanisms is that they permit the transfer property of the neural element to operate in a multimodal manner, one state supporting the usual transfer operations, the other supporting unusual transfer operations that require adaptation.

8. Cybernetic considerations relevant to a theoretical approach to analysis of neuronal adaptation in a nerve network, excerpted from a book on Memory, Learning, and Higher Function by Dr. Woody, are enclosed as an Appendix. Some aspects of that material may be summarized as follows:

An adaptive system can be described, cybernetically, as a system that modifies its internal structure as a function of experience, thereby altering the system operation. Ordinarily, the system operation will become increasingly optimized, by means of feedback, in the approach to some operational goal. In this context goal-seeking will be the process by which the component or adaptive element moves toward or maintains a particular system state. A key feature of any adaptive system will be the features controlling the adaptation. The control sub-system may or may not require associated memory. If so, the memory may evolve in a trivial or non-trivial fashion, with or without variation in the original set point. Control of goal-seeking may be expected to be accomplished by means of feedback. The latter will ordinarily involve some closed-loop operations. Interestingly, a great many psychophysiological formulations of adaptive neural systems have neglected to specify closed-loop operations by which such feedback could be accomplished as opposed to open-loop operations which do not lend themselves to modification of the involved element as a consequence of the element's past adaptation (cf. Kandel and Spencer, 1968).

Physiologically, many adaptive cellular systems lend themselves to closed-loop goal-seeking processes. These range from biochemical feedback loops (within the metabolic context of the cell itself) to recurrent collateral systems with relatively direct feedback as well as indirect feedback through more extensive polysynaptic networks (cf. Rasmussen and Goodman, 1977; Phillips, 1974). At the level of cellular components in the brain, there exist several candidate mechanisms for the control of neural adaptation:

i) The "Yin-Yang" hypothesis has been advanced in which so-called excitatory and inhibitory neurotransmitters could control closed-loop goal-seeking adaptations depending upon neuronal conductance changes by means of intracellular second messengers such as cyclic AMP and cyclic GMP. The cyclic nucleotides are thought to interact reciprocally to facilitate either excitatory or inhibitory effects (Bloom, 1975, 1976; Goldberg et al., 1973).

ii) The principle of voltage-dependent control of neuronal spike activity is well established. The possibility arises of voltage dependent induction or potentiation of cyclic nucleotide release as well as the likelihood of coupled sodium or potassium-calcium channels with voltage-dependent features (Loewenstein, 1975; Lux and Eckert, 1974; Heyer and Lux, 1976a,b).

iii) Entrainment, i.e., the production of multiple spike discharges



encroaching upon relative refractory periods, might furnish a chemical signal for cellular mechanisms controlling neural adaptation, particularly after associative stimulus pairings as in conditioning. In cortical neurons, entrainment is probabilistically an uncommon event in contrast with PSP or spike production, per se, resulting from natural auditory stimuli which serve as CS's in Pavlovian blink conditioning (Woody et al., 1970; Engel and Woody, 1972). Other evidence (Woody et al., 1976) indicates that entrainment might interact with acetylcholine or cyclic GMP to control aspects of persistent adaptation in mammalian cortical neurons.

The practical significance of using a closed-loop cybernetic approach to understand cellular adaptation, even at the biochemical level, is just beginning to be re-evaluated and appreciated. For example, the following is excerpted from a recent review by Rasmussen and Goodman (1977).

K. RASMUSSEN AND D. B. P. GOODMAN

Volume 87

July 1977

CALCIUM AND CYCLIC NUCLEOTIDES

### B. Open-Loop vs. Closed-Loop Control Systems

#### 1. General features

Nearly all models of peptide and amino hormone action, including the second-messenger model, have been ones in which a stimulus (the hormone) acts on a particular cell or subcellular system to produce a physiological response. In cybernetic terms, this is defined as an open-loop system (Fig. 2).

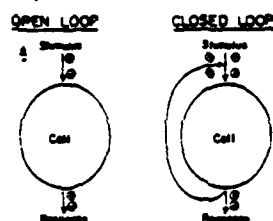


FIG. 2. Schematic representations of the contrast between open-loop and closed-loop systems in the control of cellular responses.

However, in biological systems at all levels of organization, responses are dependent not only on present and past stimuli but on the response itself, according to the present organization of the unit and its particular environment. This means that cellular responses to hormonal stimuli operate not as open- but as closed-loop systems. The distinction is critically important: in an open-loop system the response depends on the stimulus, but the converse is not true. In contrast, in a closed-loop system the response influences the stimulus—i.e., there is a feedback relationship between stimulus and response such that the response itself modifies the effect and magnitude of the original stimulus. Endocrine physiologists have realized for years that at the supracellular level endocrine systems operate as complex, closed-loop systems (327), yet most endocrine biochemists continue to analyze hormone action at the cellular level in the context of open-loop models (128, 190, 415).

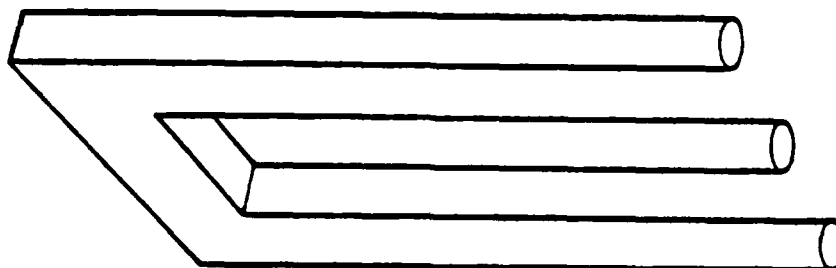
Considering these cellular control systems as closed-loop systems as schematized in Figure 2, rather than an open-loop yin-yang system as proposed by Goldberg et al. (163), adds an important dimension to both one's understanding of the system and to the types of critical experiments one can design to evaluate the hypothesis.

The importance of making this distinction in analyzing hormone action lies in the kinds of models of hormone action one builds from experimental data and from these the type of further experiments one designs to test these models. Of even greater import, if closed-loop systems are the biological rule, then an understanding of feedback theory provides a means of obtaining a correct intuitive grasp of the nature of the control system in many situations in which an open-loop analysis of the same experimental data would lead to a confusing and contradictory conclusion.

(From Physiological Reviews)

Systems of this type are of course restricted in the type of operations they can perform and the geometric patterns that can be recognized. For example, such systems cannot compute connectedness of geometric figures, whereas they can compute convexity and related processing operations of the type called local or conjunctively local by Minsky and Papert. Humans may not be able to compute some forms of connectedness either:

e.g.:



The possibility exists that a slight modification of Uttley's algorithm can result in the introduction of a self-classifying input. By self-classifying input is meant an input of particular functional significance which is identifiable, within the adaptive element, by means of its stochastic pattern of appearance alone. Moreover, this stochastic pattern need not unduly disrupt the overall function of the adaptive element's operation.

The informon model of an adaptive neural element (Uttley, 1976) incorporates classifying inputs, closed-loop feedback concerning the operational state of the element, and an appreciation of goal-seeking in the algorithm regulating useful adaptation. Several constraints are particularized that are critical if the informon is to successfully discriminate one input from another. These are a) the algorithm by which the weightings of synaptic inputs are altered, b) the need to achieve system normalization through negative (not positive) feedback of information regarding the current system state, and c) the need for a classifying input to distinguish or identify which input signal is the particular signal to be discriminated. Tests of this model have found that each of these constraints is required for the element to adapt usefully. Synaptic weighting is altered according to the Shannon mutual information function between certain synaptic inputs in combination with closed-loop negative feedback reflecting the element's internal state. In summary, it would appear that there are empirical as well as theoretical reasons why "smart" adaptive elements need to incorporate goal-seeking as well as closed-loop feedback into their design.

In some adaptive networks, input analysis, i.e., the processing of sensory-labelled information (cf. Mountcastle, 1974), is explicable in terms of the group invariance theorem of Minsky and Papert. This theorem permits analysis of operations, such as the geometry of certain sensory image processing, by algebraic means instead of statistics and thereby reverses a trend in this field. The group invariance theorem examines the relationship

between all possible receptor activations (all sets of sensory labels) and their representation across the theoretical space of an adaptive network, given certain architectural constraints. This result is a description of an orderly relationship in which no matter how complexly the network is organized, the space required for a particular sensory labelling can be specified. In summary form, the group invariance theorem states that if:

- I)  $G$  is a finite group of transformations of a finite space  $R$ ;
- II)  $\Phi$  is a set of predicates on  $R$  closed under  $G$ ;
- III)  $\Psi$  is in  $L(\Phi)$  and invariant under  $G$ .

Then there exists a linear representation of

$$\Psi = \left[ \sum_{\varphi \in \Phi} \beta_{\varphi} \varphi > 0 \right]$$

for which the coefficients  $\beta_{\varphi}$  depend only on the  $G$ -equivalence class of  $\varphi$ , that is

if  $\varphi \sim_G \varphi'$  then  $\beta_{\varphi} = \beta_{\varphi'}$ .

$L(\Phi)$  is the set of all predicates for which  $\Psi$  is a linear threshold function with respect to  $\Phi$ , and a predicate is a function that has two possible values, i.e. a binary function.

$\Psi$  is a linear threshold function with respect to  $\Phi$  ( $\Psi$  is in  $L(\Phi)$ ), if there exists a number  $\theta$ , and a set of numbers,  $\alpha_{\varphi}$  one for each  $\varphi$  in  $\Phi$ , such that:

Equation 2.6

$$\Psi(x) = \left[ \sum_{\varphi \in \Phi} \alpha_{\varphi} \varphi(x) > \theta \right]$$

## 8. Details of Research supported by AFOSR (1978-present) not covered in Part III, A.

1. The sampling distribution of neurons obtained by our intracellular, cortical recording procedure was investigated. The sample of HRP-identified neurons was found to be essentially equivalent to that seen in-situ (determined from Golgi-stained sections of these cortical regions). Seventy percent (70%) of penetrations were of cells in layers III and V, and 70% of the penetrations were of pyramidal shaped cells. There was a slight tendency to over-sample neurons with extensive dendritic arborizations. Samplings of every major morphologically identified in-situ cell type were obtained by our electrophysiological procedures (Sakai et al., Brain Res., 1978).

2. The response properties of penetrated neurons to injected polarizing currents were investigated and found to be normal. The accommodative response to ramp depolarizing currents was assessed; most responses were of the simple type rather than ceiling or minimal gradient, (cf. Koike et al., Exp. Br. Res., 1988a,b). Normal I-V plots and input resistance were also obtained. Several lines of evidence suggested that many cortical neurons have dendrites that do not support active propagation of action potentials and, instead, serve the integrative process of neuronal information handling (Woody and Gruen, Brain Res., 1978).

3. In-vitro calibrations of pressure microinjection techniques were

obtained. Controlled release of 100 femtoliter volumes was demonstrated. A number of other laboratories are adopting this technique for testing local biologic effects of pharmacologic agents (cf. Sakai et al., Neuropharmacol., 1979).

4. Preliminary evaluations of effects of acetylcholine (ACh) and cyclic GMP (cGMP) on cortical neurons were completed. These agents appear to have similar effects on input resistance, ACh acting extracellularly on cell surface receptors (of muscarinic type), cGMP acting intracellularly. The input resistance is increased transiently by the effect of these agents alone and persistently by application with cell depolarization sufficient to produce repeated discharge (Woody et al., Brain Res., 1978).

It appears that neurotransmitters act in a dual manner in these cells, as in others, to convey information. One action, the direct "neurotransmitter effect", serves primarily to transmit information through the cell. The other action, the "modulatory effect", serves to control adaptation as a function of the information transmitted. The two actions are kept separated in the time-frequency domain by different time courses of involved biochemical pathways; [see Klopff, A.H., Brain Function and Adaptive Systems — A Heterostatic Theory, AFCRL Dept., HI33, 1972].

A third variable, depolarization included discharge, serves to make the adaptation persistent rather than transient.

5. In a simulated neuron, consequences of propagative vs. non-propagative dendritic membranes on information transfer were studied. With low rates of current spread, graded changes in threshold produced graded changes in output discharge. With high rates of current spread, the neuron became a bistable (decisional) operator where spiking was enhanced if the threshold was below a certain level and suppressed if above that level. The enhancement was considerably more pronounced in neurons with non-propagative than with propagative dendrites. With propagative dendrites a less intense input was needed to initiate somatic spiking (Levine and Woody, Biol. Cybernetics, 1978).

6. Studies of the ability to morphologically identify types of neurons responding to cholinergic agents were conducted using aceclidine, a cholinomimetic drug. Similar effects on membrane resistance were obtained with this drug as with ACh and the effects could be blocked by atropine (a muscarinic receptor blocker). A cell responding to aceclidine with an increased resistance was identified by injection of HRP as a pyramidal cell of layer VI (Swartz et al., Proc. West. Pharm. Soc., 1978).

7. Effects of acetylcholine (ACh) and cyclic GMP (cGMP) on input resistance were studied in groups of morphologically identified neurons. HRP was pressure injected into the cells after studying the effects of ACh. cGMP was also applied intracellularly by pressure injection. Pyramidal cells of layers V and VI responded to these agents with increases in resistance. The responsive neurons included those of layer V activated antidromically by PT stimulation.

A comparison of the results of pressure injected cGMP with those of intracellularly iontophoresed cGMP shows similar changes in resistance, but the

increase in firing rate after the hyperpolarizing iontophoresis does not occur after pressure injection. The results suggest that cGMP and acetylcholine produce similar effects in similar neurons of the motor cortex, the primary effect being a conductance decrease. The increase in firing rate following application of acetylcholine appears to be a separate effect of this agent, apart from that supported by cGMP as a second messenger. This effect may arise from excitation of surrounding neurons presynaptic to the one recorded or from other, direct conductance effects of acetylcholine binding at the neuronal receptors. (Swartz and Woody, J. Neurobiol., 1979; Woody et al., Soc. Neurosci. Abstr., 1979).

8. The effects of two separate unconditioned stimuli (US) on cortical neurons were studied.

a. Behavioral US (glabella tap)

The excitability of cortical neurons to intracellularly injected current (depol., 10 ms, 10 Hz pulses) was compared in cats given US alone in training and testing versus cats given auditory stimuli (click) and cats given US in training but not in testing. There were no differences in neural excitability in the latter 2 groups, but less current was required to discharge cells in cats given US during training and testing. Reference to additional control studies indicates that the excitability of neurons of the motor cortex to intracellularly applied current was transiently increased by US presentation.

The effects of US presentation on unit discharge were also assessed (Table I). The predominant effect of US delivery on cortical neurons was IPSP production and a reduction in rates of discharge; however on Day 2 of US presentations, significant increase was observed in the numbers of cells responding with increased rates of discharge to US delivery.

Thus, evidence has been found for three US effects: 1) a transient increase in intracellular excitability lasting hours or days but not weeks, 2) a decrease in extracellular excitability of unknown duration and 3) an increase in the numbers of cells activated to discharge by the US from Day 1 to 2 of serial US presentation. (Brons, J., Doctoral Thesis, UCLA, 1979).

b. Antidromic US

Antidromic stimulation of the pyramidal tract has been used successfully as a US to produce conditioned learning (O'Brien et al., 1977). Effects of low frequency 4-8 Hz PT stimulation (stereotax cord: F 3.5, L 4.0, H 4.5) on cortical neurons were investigated. Cortical cells activated antidromically responded predominantly with reduced excitability to intracellularly applied current. Cortical cells activated transsynaptically responded with increased intracellular excitability. Those cells failing to respond showed no change in excitability during the 5-15 minutes tested. (Tzebelikos and Woody, Brain Res. Bull., 1979).

A comparison of these results with those of high frequency stimulation (usually > 50 Hz) reported by Bindman et al. (J. Physiol., 1979) is shown in Table II. As indicated, the direction of change is frequency dependent and differs between antidromically and transsynaptically activated units.

TABLE I

Percent of cells responding with increased discharge (E), decreased discharge (I) or failing to respond (UR) to glabella tap US on days 1 and 2 of repeated US presentations. Numbers of cells tested (n) are shown to the right.

	E	I	UR	n
Day 1	29%	36%	35%	55
Day 2	*55%	27%	18%	73

\*difference significant, Chi sq.  $p < .025$

TABLE II

Comparison of effects of high and low frequency  
PT stimulation on cortical neural excitability.

Low Frequency (Woody)

Antidromically activated:	excitability ↓
Transsynaptically activated:	excitability ↑
Unresponsive:	no change

High Frequency (Bindman, et al.)

Antidromically activated:	excitability ↑
Transsynaptically activated:	excitability ↓

Numbers of cells responding to low frequency  
stimulation:

	<u>Excitability ↓</u>	<u>Excitability ↑</u>	<u>No change</u>
Antidromic	14	9	11
Transsynaptic	6	21	15
Unresponsive	1	2	37

## REFERENCES

- Berthier, N.E., Betts, B., and Woody, C.D. Discriminative conditioning of eyeblink with aversive brain stimulation. Soc. Neurosci. Abstr. 8: 315, 1982.
- Bindman, L.J., Lippold, O.C.J., and Milne, A.R. Prolonged changes in excitability of pyramidal tract neurones in the cat: a postsynaptic mechanism. J. Physiol. (Lond.) 286: 457-477, 1979.
- Bindman, L., Woody, C., Gruen, E., and Betts, B. PT stimulation produces conductance decrease IPSPs in neurons of the motor cortex of cats. Soc. Neurosci. Abstr. 8: 540, 1982.
- Bloom, F.E. The role of cyclic nucleotides in central synaptic function. Rev. Physiol. Biochem. Pharmacol. 74: 1-103, 1975.
- Bloom, F.E. The role of cyclic nucleotides in central synaptic function and neuron-target cell interactions. Neurosciences Res. Prog. Bull. 14: 377-386, 1976.
- Brons, J. Doctoral thesis. UCLA, 1979.
- Brons, J., Woody, C.D., and Allon, N. Changes in the excitability to weak intensity electrical stimulation of units of the pericruciate cortex in cats. J. Neurophysiol. 47: 377-388, 1982.
- Engberg, I. and Marshall, K.C. Mechanism of noradrenaline hyperpolarization in spinal cord motoneurons of the cat. Acta Physiol. Scand. 83: 142-144, 1971.
- Engel, J., Jr. and Woody, C.D. Effects of character and significance of stimulus on unit activity at coronal - pericruciate cortex of cat during performance of conditioned motor response. J. Neurophysiol. 35: 220-229, 1972.
- Goldberg, N.D., Haddox, M.K., Estensen, R., Lopez, C. and Hadden, J.W. Evidence for a dualism between cyclic GMP and cyclic AMP in the regulation of cell proliferation and other cellular processes. In: Cyclic AMP, Cell Growth and Immune Response, edited by W. Braun, L.M. Lichtenstein and C.W. Parker. Springer-Verlag, New York, 1973.
- Heyer, C.B. and Lux, H.D. Properties of a facilitating calcium current in pacemaker neurones of the snail, Helix pomatia. J. Physiol. 262: 319-348, 1976a.
- Heyer, C.B. and Lux, H.D. Control of the delayed outward potassium currents in bursting pacemaker neurones of the snail, Helix pomatia. J. Physiol. 262: 349-352, 1976b.
- Kandel, E.R. and Spencer, W.A. Cellular neurophysiological approaches in the study of learning. Physiol. Rev. 48: 65-134, 1968.
- Kim, E.H.-J., Woody, C.D., and Berthier, N.E. Rapid acquisition of conditioned eye blink responses in cats following pairing of an auditory CS with



- glabella tap US and hypothalamic stimulation. J. Neurophysiol. 49: 767-779, 1983.
- Klopf, A.H. Brain Function and Adaptive Systems - A Heterostatic Theory. Air Force Cambridge Laboratories Research. AFCRL-72-0164, 1972.
- Koike, H., Okada, Y., Oshima, T. and Takahashi, K. Accommodative behavior of cat pyramidal tract cell investigated with intracellular injection of currents. Exp. Br. Res. 5: 173-188, 1968a.
- Koike, H., Okada, Y. and Oshima, T. Accommodative properties of fast and slow pyramidal tract cells and their modification by different levels of their membrane potential. Exp. Brain Res. 5: 189-201, 1968b.
- Levine, D.S. and Woody, C.D. Effects of active versus passive dendritic membranes on the transfer properties of a simulated neuron. Biol. Cybernetics, 31: 63-70, 1978.
- Loewenstein, W.R. Permeable Junctions. In: Symposium on Quantitative Biology. Cold Spring Harbor, 1975.
- Lux, H.D. and Eckert, R. Inferred slow inward current in neurones. Nature (Lond.) 250: 547-576, 1974.
- Mountcastle, V.D., ed. Intensity functions and linearity of transmission in lemniscal system. In: Medical Physiology, Volume 1, St. Louis, MO, C.V. Mosby Company, 1974, pp. 329-330ff.
- O'Brien, J.H., Wilder, M.B. and Stevens, C.D. Conditioning of cortical neurons in cat with antidromic activation as the unconditional stimulus. J. Comp. Physiol. Psychol. 91: 918-929, 1977.
- Phillips, C.G. The cerebral cortical stage of movement control. Proc. Intl. Union Physiol. Sci. 10: 142, 1974.
- Rasmussen, H. and Goodman, D.B.P. Relationships between calcium and cyclic nucleotides in cell activation. Physiol. Rev. 57: 421-509, 1977.
- Sakai, M., Sakai, H. and Woody, C. Sampling distribution of morphologically identified neurons of the coronal- pericruciate cortex of awake cats following intracellular injection of HRP. Brain Res. 152: 329-333, 1978.
- Sakai, M., Swartz, B.E. and Woody, C.D. Controlled microrelease of pharmacologic agents: measurements of volume ejected in vitro through fine tipped glass microelectrodes by pressure. Neuropharmacol. 18: 209-213, 1979.
- Siggins, G.R., Hoffer, B.J. and Bloom, F.E. Studies on norepinephrine containing afferents to Purkinje cells of rat cerebellum. III. Evidence for mediation of norepinephrine effects by cyclic 3', 5'- adenosine monophosphate. Brain Res. 25: 535-553, 1971.
- Swartz, B.E. and Woody, C.D. Correlated effects of acetylcholine and cyclic guanosine monophosphate on membrane properties of mammalian neocortical

- neurons. J. Neurobiol. 10: 465-488, 1979.
- Swartz, B.E., Woody, C.D. and Jenden, D.J. The effects of aceclidine, a muscarinic agonist on neurons in the sensorimotor cortex of awake cats. Proc. West. Pharm. Soc. 21: 11-17, 1978.
- Tzebelikos, E. and Woody, C.D. Intracellularly studied excitability changes in coronal-pericruciate neurons following low frequency stimulation of the corticobulbar tract. Brain Res. Bull. 4: 635-641, 1979.
- Uttley, A.M. A two-pathway informon theory of conditioning and adaptive pattern recognition. Brain Res. 102: 23-35, 1976.
- Wallis, R.A., Woody, C.D., and Gruen, E. Effects of intracellular pressure injections of calcium ions in morphologically identified neurons of cat motor cortex. Soc. Neurosci. Abstr. 8: 909, 1982.
- Woody, C.D. Acquisition of conditioned facial reflexes in the cat: cortical control of different facial movements. Fed. Proc. 41: 2160-2168, 1982.
- Woody, C.D. and Gruen, E. Characterization of electrophysiological properties of intracellularly recorded neurons in the neocortex of awake cats: a comparison of the response to injected current in spike overshoot neurons. Brain Res. 158: 343-357, 1978.
- Woody, C.D., Kim, E.H.-J., and Berthier, N.E. Effects of hypothalamic stimulation on unit responses recorded from neurons of sensorimotor cortex of awake cats during conditioning. J. Neurophysiol. 49: 780-791, 1983.
- Woody, C.D., Knispel, J.D., Crow, T.J. and Black-Cleworth, P. Activity and excitability to electrical current of cortical auditory receptive neurons of awake cats as affected by stimulus association. J. Neurophysiol. 39: 1045-1061, 1976.
- Woody, C.D., Sakai, H., Swartz, B., Sakai, M. and Gruen, E. Responses of morphologically identified mammalian, neocortical neurons to acetylcholine (ACh), aceclidine (Acec), and cyclic GMP (cGMP). Soc. Neurosci. Abstr. 5: 601, 1979.
- Woody, C.D., Swartz, B.E. and Gruen, E. Effects of acetylcholine and cyclic GMP on input resistance of cortical neurons in awake cats. Brain Res. 158: 373-395, 1978.
- Woody, C.D., Vassilevsky, N.N. and Engel, J. Jr. Conditioned eyeblink: unit activity at coronal-pericruciate cortex of the cat. J. Neurophysiol. 33: 851-864, 1970.

IV. PUBLICATIONS SUPPORTED BY AFOSR

## A. 1982 - Present

1. Brons, J., Woody, C.D., and Allon, N. Changes in the excitability to weak intensity electrical stimulation of units of the pericruciate cortex in cats. J. Neurophysiol. 47:377-388, 1982.
2. Woody, C.D. Acquisition of conditioned facial reflexes in the cat: cortical control of different facial movements. Fed. Proc. 41:2160-2168, 1982.
3. Berthier, N.E., Betts, B., and Woody, C.D. Discriminative conditioning of eyeblink with aversive brain stimulation. Soc. Neurosci. Abstr. 8:315, 1982.
4. Bindman, L., Woody, C.D., Gruen, E., and Betts, B. PT stimulation produces conductance IPSPs in neurons of the motor cortex of cats. Soc. Neurosci. Abstr. 8:540, 1982.
5. Wallis, R.A., Woody, C.D., and Gruen, E. Effects of intracellular pressure injections of calcium ions in morphologically identified neurons of cat motor cortex. Soc. Neurosci. Abstr. 8:909, 1982.
6. Woody, C.D. (Ed.) Conditioning: Representation of Involved Neural Functions. Plenum Press, New York, 1982.
7. Woody, C.D. Neurophysiological correlates of latent facilitation. In: Woody, C.D. (Ed.) Conditioning: Representation of Involved Neural Functions. Plenum Press, New York, 1982, pp. 233-248.
8. Woody, C.D. Memory, Learning, and Higher Function. Springer-Verlag, New York, 1982.
9. Kim, E.H.-J., Woody, C.D., and Berthier, N.E. Rapid acquisition of conditioned eyeblink responses in cats following pairing of an auditory CS with glabella tap US and hypothalamic stimulation. J. Neurophysiol. 49: 767-779, 1983.
10. Woody, C.D., Kim, E.H.-J., and Berthier, N.E. Effects of hypothalamic stimulation on unit responses recorded from neurons of the sensorimotor cortex of awake cats during conditioning. J. Neurophysiol. 49: 780-791, 1983.
11. Berthier, N.E. and Woody, C.D. An essay on latent learning. In: The Neuropsychology of Memory, N. Butters and L.R. Squire (Eds.). Guilford Press, New York, 1983, in press.
12. Woody, C.D. Studies of Pavlovian eyeblink conditioning in awake Cats. In: Proceedings of the Conference on the Neurobiology of Learning and Memory, G. Lynch, N. Weinberger, and J.L. McGaugh (Eds.). Guilford Press, New York, 1983, in press.

## B. 1976 - 1981

1. Woody, C.D. Alterations in neuronal excitability supporting sensorimotor

- integration. Proc. Intl. Union Physiol. Sci. 12: 604, 1977.
2. Sakai, M., Sakai, H. and Woody, C. Identification of intracellularly recorded neocortical neurons by intracellular pressure microinjection of horseradish peroxidase (HRP) and in vivo biopsy. Fed. Proc. 36: 1294, 1977.
  3. Woody, C.D. If cyclic GMP is a neuronal second messenger, what's the message? In: Cholinergic Mechanisms and Psychopharmacology, D.E. Jenden, (Ed.) Plenum, New York, 1977, pp. 253-259.
  4. Woody, C.D., Swartz, B.E. and Gruen, E. Persistent, correlated effects of acetylcholine (ACh) and Cyclic GMP (cGMP) on input resistance of neocortical neurons of awake cats. Proc. Intl. Union Physiol. Sci. 13: 820, 1977.
  5. Sakai, M., Sakai, H. and Woody, C. Intracellular staining of cortical neurons by pressure microinjection of horseradish peroxidase and recovery by core biopsy. Exp. Neurol. 58: 138-144, 1978. (a)
  6. Sakai, M., Sakai, H. and Woody, C.D. Sampling distribution of intracellularly recorded cortical neurons identified by injection of HRP. Fed. Proc. 37: 251, 1978.
  7. Woody, C.D. A possible role for cyclic GMP (cGMP) as an intracellular messenger for acetylcholine (ACh) at muscarinic synapses in the mammalian cortex. In: Iontophoresis and Transmitter Mechanisms in the Mammalian Central Nervous System, R.W. Ryall and J.S. Kelly, Eds. Elsevier/North Holland, Inc., New York, 1978.
  8. Sakai, M., Swartz, B.E. and Woody, C.D. Measurements of volume ejected in vitro through fine tipped glass microelectrodes by the pressure microinjection technique. Western Nerve Net Abst., 1978.(c)
  9. Sakai, M., Sakai, H. and Woody, C. Sampling distribution of morphologically identified neurons of the coronal-pericruciate cortex of awake cats following intracellular injection of HRP. Brain Res. 152: 329-333, 1978.
  10. Woody, C.D. and Gruen, E. Characterization of electrophysiological properties of intracellularly recorded neurons in the neocortex of awake cats: a comparison of the response to injected current in spike overshoot neurons. Brain Res. 158: 343-357, 1978.
  11. Sakai, M., Swartz, B.E. and Woody, C.D. Controlled microrelease of Oxpharmacologic agents: measurements of volume ejected in vitro through fine tipped glass microelectrodes by pressure. Neuropharmacol. 18: 209-213, 1979.
  12. Woody, C.D., Swartz, B.E. and Gruen, E. Effects of acetylcholine and cyclic GMP on input resistance of cortical neurons in awake cats. Brain Res. 158: 373-395, 1978.
  13. Swartz, B.E., Woody, C.D. and Jenden, D.J. The effects of aceclidine, a muscarinic agonist on neurons in the sensorimotor cortex of awake cats. Proc. West. Pharm. Soc. 21: 11-17, 1978.

14. Levine, D.S. and Woody, D.C. Effects of active versus passive dendritic membranes on the transfer properties of a simulated neuron. Biol. Cybernetics 31: 63-70, 1978.
15. Tzebelikos, E. and Woody, C.D. Intracellularly studied excitability changes in coronal-pericruciate neurons following low frequency stimulation of the cortobulbar tract. Brain Res. Bull. 4: 635-641, 1979.
16. Swartz, B.E. and Woody, C.D. Correlated effects of acetylcholine and cyclic guanosine monophosphate on membrane properties of mammalian neurocortical neurons. J. Neurobiol. 10: 465-488, 1979.
17. Woody, C.D., Sakai, H., Swartz, B., Sakai, M., and Gruen, E. Responses of morphologically identified mammalian, neocortical neurons to acetylcholine (ACh), aceclidine (Acec) and cyclic GMP (cGMP). Soc. Neurosci. Abstr. 5: 601, 1979.
18. Kim, H-J. and Woody, C.D. Facilitation of eye-blink conditioning by hypothalamic stimulation. Soc. Neurosci. Abstr. 5: 319, 1979.
19. Brons, J. and Woody, C.D. Changes in responsiveness to glabella tap among neurons in the sensorimotor cortex of awake cats. Soc. Neurosci. Abstr. 5: 314, 1979.
20. Sakai, H. and Woody, C.D. Identification of auditory responsive cells in the coronal-pericruciate cortex of awake cats. J. Neurophysiol. 44: 223-231, 1980.
21. Nahvi, M.J., Woody, C.D., Tzebelikos, E., and Ribak, C.E. Electrophysiological characterization of morphologically identified neurons in the cerebellar cortex of awake cats. Exp. Neurol. 67: 368-376, 1980.
22. Ribak, C.E., Woody, C.D., Nahvi, M.J., and Tzebelikos, E. Ultrastructural identification of physiologically recorded neurons in the cat cerebellum. Exp. Neurol. 67: 377-390, 1980.
23. Brons, J.F. and Woody, C.D. Long-term changes in excitability of cortical neurons after Pavlovian conditioning and extinction. J. Neurophysiol. 44: 605-615, 1980.
24. Woody, C.D. and Gruen, E. Effects of cyclic nucleotides on morphologically identified cortical neurons of cats. Proc. Int. Union Physiol. Sci. 14: 789, 1980.
25. Woody, C.D., Ribak, C.E., Sakai, M., Sakai, H., and Swartz, B. Pressure microinjection for the purposes of cell identification and subsequent ultramicroscopic analysis. In: Current Trends in Morphological Techniques, Vol. II (Ed. J.E. Johnson, Jr.), CRC Press, Inc., 1981.
26. Woody, C.D. Studies of conditioning and other forms of adaptation in the mammalian CNS, In: Cellular Analogues of Conditioning and Neural Plasticity Ed. Fehér, O., and Joo, F. Advances in Physiological Science, Pergamon Press and Akademiai Kiado, Oxford, 36: 117-128, 1981.

27. Berthier, N.E., Betts, B., and Woody, C.D. Rapid conditioning of eyeblink reflex: response topography. Soc. Neurosci. Abstr. 7:750, 1981.

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1957 - A.B. Princeton University  
1962 - M.D. Harvard Medical School (Magna Cum Laude)

## Positions Held:

1977 - Professor, Anatomy, Psychiatry and Biobehavioral Science,  
UCLA (in Residence)

1982 (summer) Research Scientist, Marine Biological Laboratory, Woods Hole,  
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1976 - 1977 Associate Professor in Residence of Anatomy and Psychiatry,  
University of California at Los Angeles

1971 - 1976 Associate Professor in Residence of Anatomy, Physiology, and  
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1968 - 1971 Research Officer (permanent), Laboratory of Neural Control,  
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1967 - 1968 Harvard Moseley Fellow with Dr. Jan Bures, Institute of  
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1962 - 1963 Intern in Medicine, Strong Memorial Hospital, University of  
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1960 - 1961 NIH Post-sophomore Research Fellow at Stanley Cobb  
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 Honorary Member, Pavlovian Institute, U.S.S.R., 1972  
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 Member, Brain Research Institute, and Mental Retardation Research Center, UCLA  
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 Chairman, Session on "Brain and Behavior", FASEB Annual Meeting, 1973  
 Chairman, Session on "Behavior and Conditioning", International Congress of Physiological Science, New Delhi, 1974  
 Invited Research Scientist and Lecturer at Kyoto University Primate Center, Japan; sponsored by Japan Society for the Promotion of Science, 1975  
 Chairman, Session on "Behavior and Neuroethology", FASEB Annual Meeting, 1977  
 Invited Panelist, Session on "Association Systems and Sensorimotor Integration", International Physiological Congress, Paris, 1977  
 Chairman, Session on "Neurotransmitters", Soc. for Neuroscience, October, 1979.  
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- Recent Research:
1. Changes in excitability of units in cat pericruciate cortex to weak extracellular stimulation during conditioning
  2. The ionic mechanism underlying the excitation of cells in the motor cortex by weak extracellular currents

## PUBLICATIONS:

Allon, N. and Kochva, E. (1972) Amount of venom injected into mice and rats by Vipera palaestina in a single bite. Am. Zool. 12:685.

Kochva, E., Oron, U., Bdolah, A., and Allon, N. (1972) Regulacao da secrecao e injecao de venamo em sepentes viperideos. Simposio: "Aplicacao de venenos das serpentes em Problemas de Farmacologia e Bioquimica celular". Ribeirao Preto S.P. Brazil.

- Allon, N. and Kochva, E. (1974) The quantities of venom injected into prey of different sizes by Vipera palaestina in a single bite. J. Exp. Zool. 188:71-76.
- Kochva, E., Oron, U., Bdolah, A., and Allon, N. (1975) Regulation of venom secretion and injection in viperid snakes. Toxikon 13:104.
- Allon, N. and Wollberg, Z. (1978a) Superior colliculus of squirrel monkey: Responses of single cells to auditory stimuli. Abstract presented in the Israel Society of Physiology and Pharmacology.
- Allon, N. and Wollberg, Z. (1978b) Responses of cells in the medial geniculate body (MGB) of squirrel monkey to auditory stimuli. Neurosci. Ltrs. Suppl. 1:52.
- Allon, N. and Wollberg, Z. (1980) The response properties of cells in the medial geniculate body (MGB) of awake squirrel monkey to species specific vocalization. Soc. Neurosci. Abstr. 6:333.
- Allon, N., Yeshurun, Y., and Wollberg, Z. (1981) Responses of single cells in the medial geniculate body of awake squirrel monkey. Exp. Brain Res. 41:222-232.
- Yeshurun, Y., Allon, N., and Wollberg, Z. (1981) A computer aided simulation of an electrode penetration into deep brain structures. Computers and Biomed. Res. 14:19-31.
- Brons, J.F., Woody, C.D., and Allon, N. (1982) Changes in the excitability to weak intensity extracellular electrical stimulation of units of the pericruciate cortex in cats. J. Neurophysiol. 47:377-388.
- Allon, N., and Woody, C.D. (1982) Initiation of paroxysmal depolarization shifts in single cells of the sensorimotor cortex of awake cats by scorpion venom (Centruroides sculpturatus). Soc. Neurosci. Abstr. 8:101.
- Allon, N., and Woody, C.D. Epileptiform activity induced in single cells of the sensorimotor cortex of the cat by intracellularly applied scorpion venom (Centruroides sculpturatus). Exp. Neurol., 1983, in press.

# Curriculum Vita

Neil E. Berthier

April 1983

PII Redacted

## II. Educational Background:

- A. Attended University of Massachusetts, Amherst, Ma. from September 1975 to November 1980. M.S. May, 1978, Ph.D. February, 1981. Psychology, concentration in Neurobiology of Learning and Memory, Advisor J.W. Moore.
- B. Attended Virginia Polytechnic Institute and State University, Blacksburg, Va. from September 1971 to March, 1975. B.S. June 1975 with Distinction in Psychology.
- C. Graduate Courses Taken:
  - Statistical Inference in Psychology
  - Physiological Psychology
  - Neuroanatomy
  - Advanced Applied Statistics
  - Conditioning
  - Comparative Neurophysiology
  - Psychopharmacology
  - Animal Learning
  - Human Information Processing
  - Neurobiology of Learning and Memory
  - Developmental Neurobiology
  - Experimental Neurophysiology
- Courses Audited:
  - Calculus I, II, and Multivariate Calculus
  - Minicomputers
  - Neurochemistry
- D. Student in the January 1982 Neurobiology course at the Marine Biological Laboratory, Woods Hole, Ma.

## III. Professional Positions:

- A. Assistant Research Neurobiologist, January, 1981 to present, Department of Psychiatry, Mental Retardation Research Center, Neuropsychiatric Institute, UCLA Medical Center, Los Angeles, Ca

B. Teaching Assistant and Associate, September 1975 to May 1980, University of Massachusetts, Amherst Ma. Assisted and prepared exams and lectures for courses in Physiological Psychology, Animal Learning, Statistics, Methods, and Introductory Psychology.

IV. Professional Specialties and memberships:

Neurobiology of Learning and Memory, Animal Learning.

Member of the Society for Neuroscience

V. References:

Dr. J.W. Moore, Department of Psychology,  
University of Massachusetts, Amherst Ma. 01003

Dr. C.D. Woody, Departments of Psychiatry and Anatomy  
University of California Los Angeles, Los Angeles, Ca. 90024

Dr. D.L. Alkon, Laboratory of Biophysics, Marine Biological  
Laboratory, Woods Hole, Ma. 02543

Dr. G.A. Wyse, Department of Zoology,  
University of Massachusetts, Amherst Ma. 01003

VI. Publications and Presentations:

Berthier, N.E., Spinelli, D.N., Solomon, P.R. & Moore, J.W.  
Fiber-sparing lesions of the central nervous system produced by cyanide. Presented by Moore at the European Brain and Behavior Society's workshop on the Cerebral Commissures. Rotterdam, March, 1977.

Moore, J.W., Yeo, C. & Berthier, N.E. Brain mechanisms of Pavlovian inhibition. Presented at the Annual meeting of the Psychonomic Society, San Antonio, 1978.

Powell, G.M., Berthier, N.E. & Moore, J.W. Efferent neuronal control of the nictitating membrane in rabbit (*Oryctolagus cuniculus*): A reexamination. *Physiology & Behavior*, 1979, 23, 299-308.

Berthier, N.E. & Moore, J.W. Role of the extraocular muscle in rabbit (*Oryctolagus cuniculus*) nictitating membrane response. *Physiology & Behavior*, 1980, 24, 931-937.

Berthier, N.E. & Moore, J.W. Spatial differential conditioning of the nictitating membrane response in hippocampectomized rabbits. *Physiological Psychology*, 1980, 8, 451-454.

Berthier, N.E. & Moore, J.W. Disrupted conditioned inhibition of the rabbit nictitating membrane response following mesencephalic lesions. *Physiology & Behavior*, 1980, 25, 667-673.

- Berthier, N.E. & Moore, J.W. Multiple unit activity of the abducens nerve in the anesthetized and paralyzed rabbit. Society for Neuroscience Abstracts, 1980, 6, 427.
- Berthier, N.E., Betts, B. & Woody, C.D. Rapid eyeblink conditioning: response topography. Society for Neuroscience Abstracts, 1981, 7, 750.
- Desmond, J.E., Berthier, N.E. & Moore, J.W. Brains stem elements essential for the classically conditioned nictitating membrane response of rabbit. Society for Neuroscience Abstracts, 1981, 7, 650.
- Moore, J.W., Berthier, N.E. & Desmond, J.E. Brain stem electrophysiological correlates of the classically conditioned nictitating membrane response in rabbit. Society for Neuroscience Abstracts, 1981, 7, 358.
- Moore, J.W., Desmond, J.E. & Berthier, N.E. The metencephalic basis of the conditioned nictitating membrane response. In Conditioning: Representation of Involved Neural Functions. C.D. Woody (Ed.), New York: Plenum, 1982.
- Berthier, N.E., Betts, B. & Woody, C.D. Discrimination conditioning of eyeblink with aversive brain stimulation. Society for Neuroscience Abstracts, 1982, 8, 315.
- Berthier, N.E. & Moore, J.W. The unconditioned nictitating membrane response: The role of the abducens nerve and nucleus and the accessory abducens nucleus in the rabbit, Brain Research, 1983, 258, 201-210.
- Kim, E.H-J., Woody, C.D. & Berthier, N.E. Rapid acquisition of conditioned eyeblink responses in cats following pairing of an auditory conditioned stimulus with glabella tap unconditioned stimulus and hypothalamic stimulation, Journal of Neurophysiology, 1982, 49, 767-779.
- Woody, C.D., Kim, E.H-J. & Berthier, N.E. Effects of hypothalamic stimulation on unit responses recorded from neurons of the sensorimotor cortex of awake cats during conditioning, Journal of Neurophysiology, 1982, 49, 780-791.

Name: Dr. Lynn J. Bindman (née Winton)

Address: Department of Physiology  
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Education: South Hampstead High School for Girls, London  
University College London. Department of Physiology  
1957-1963

Degrees: BSc London 1960 Class Upper II  
PhD London 1964 Physiology of the cerebral cortex

Posts held: Honorary Research Assistant, Department of Physiology,  
UCL, Grant awarded by Medical Research Council 1963-1965

Assistant Lecturer (part-time) Department of Physiology,  
UCL 1965-1969

Research Associate (part-time) Department of Physiology,  
UCL. Grant awarded by Medical Research Council 1969-1972

Lecturer, Department of Physiology, UCL 1972-

Membership of Societies

The Physiological Society	- elected 1967
Education sub-committee	- appointed 1981
The Pharmacological Society	- elected 1976
International Brain Research Organisation	- elected 1978
Brain Research Association	

Research:

- LIPPOLD, O.C.J., REDFEARN, J.W.T. & WINTON, L.J. (1961). The potential level at the surface of the cerebral cortex of the rat and its relation to the cortical activity evoked by sensory stimulation. J. Physiol., 157, 7-9P
- BINDMAN, L.J., LIPPOLD, O.C.J. & REDFEARN, J.W.T. (1961). The diffusion of  $\gamma$ -amino butyric acid within the mammalian cerebral cortex and the non-selective nature of its blocking action. J. Physiol., 160, 24-25P
- BINDMAN, L.J., LIPPOLD, O.C.J. & REDFEARN, J.W.T. (1962). The prolonged after-action of polarizing currents on the sensory cerebral cortex. J. Physiol., 162, 45-46P
- BINDMAN, L.J., LIPPOLD, O.C.J. & REDFEARN, J.W.T. (1962). Long-lasting changes in the level of the electrical activity of the cerebral cortex produced by polarizing currents. Nature, 196, 584-585
- BINDMAN, L.J., LIPPOLD, O.C.J. & REDFEARN, J.W.T. (1962). Variations in evoked potentials and potential gradients in the sensory cortex. Proc. XXII Int. Congr. Physiol. Sci., Leiden, Sept. 10-17
- BINDMAN, L.J., LIPPOLD, O.C.J. & REDFEARN, J.W.T. (1962). The non-selective blocking action of  $\gamma$ -amino butyric acid on the sensory cerebral cortex of the rat. J. Physiol., 162, 105-120
- BINDMAN, L.J., LIPPOLD, O.C.J. & REDFEARN, J.W.T. (1963). Comparison of the effects on electrocortical activity of general body cooling and local cooling of the surface of the brain. Electroenceph. clin. Neurophysiol. 15, 238-245
- BINDMAN, L.J., LIPPOLD, O.C.J. & REDFEARN, J.W.T. (1964). Relation between the size and form of potentials evoked by sensory stimulation and the background electrical activity in the cerebral cortex of the rat. J. Physiol., 171, 1-25
- \* BINDMAN, L.J., LIPPOLD, O.C.J. & REDFEARN, J.W.T. (1964). The action of brief polarizing currents on the cerebral cortex of the rat (1) during current flow and (2) in the production of long-lasting after-effects. J. Physiol., 172, 369-382
- BINDMAN, L.J. (1964) Evoked potentials and background electrical activity in the cerebral cortex. Ph.D. Thesis University of London.
- BINDMAN, L.J. (1965) Long-lasting changes in the firing frequency of neurones in the rat cerebral cortex and radial potential gradients. J. Physiol., 179, 14-16P.
- BINDMAN, L.J. & BOISACQ-SCHEPENS, N. (1966). Persistent changes in the rate of firing of single, spontaneously active cortical cells in the rat produced by peripheral stimulation. J. Physiol., 185, 14-17P



BINDMAN, L.J. & BOISACQ-SCHEPENS, N. (1967). The relation between the 'spontaneous' rate of firing of neurones in the rat's cerebral cortex, their response to peripheral stimulation, and the duration of the after-discharge following stimulus. J. Physiol., 191, 7-9P

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BOISACQ-SCHEPENS, N., & BINDMAN, L.J. (1967). Modifications durable, par la stimulation somatique, de la fréquence de décharge spontanée de neurones corticaux chez le Rat: Différences entre les voies assurant l'excitation primaire et l'activation prolongée. J. Physiologie (Paris), 59, 355-356.

BINDMAN, L.J. & RICHARDSON, H.R. (1969) Persisting changes in the firing pattern of single cortical units responding at short latency to weak somatic stimuli in the anaesthetized rat. J. Physiol., 202, 53-55P

BINDMAN, L.J., BOISACQ-SCHEPENS, N. & RICHARDSON, H.R. (1971) "Facilitation" and "Reversal of response" of neurones in the cerebral cortex. Nature New Biology, 230, 216-218

BINDMAN, L.J., LIPPOLD, O.C.J. & MILNE, A.R. (1976). Long-lasting changes of post-synaptic origin in the excitability of pyramidal tract neurones J. Physiol., 258, 71-72P

BINDMAN, L.J., LIPPOLD, O.C.J., & MILNE, A.R. (1976). Prolonged decreases in excitability of pyramidal tract neurones. J. Physiol., 263, 141-142P.

BINDMAN, L.J. & RICHARDSON, H.R. (1976). Enhancement of a phase of reduced firing in the response of spontaneously active cortical neurones to somatic stimulation. J. Physiol., 263, 262-263P

BINDMAN, L.J. & MILNE, A.R. (1977) The reversible blocking action of topically applied magnesium solutions on neuronal activity in the cerebral cortex of the anaesthetized rat. J. Physiol., 269, 34-35P

\* BINDMAN, L.J., LIPPOLD, O.C.J. & MILNE, A.R. (1979) Prolonged changes in excitability of pyramidal tract neurones in the cat: a postsynaptic mechanism. J. Physiol., 286, 457-477

BINDMAN, L.J. & MOORE, R.B. (1980) The effect of cycloheximide on the production of prolonged increases in firing rate of cortical neurones by somatic stimulation in the anaesthetized rat. J. Physiol., 305, 34-35P.

BINDMAN, L.J., LIPPOLD, O.C.J. & MILNE, A.R. (1981) A post-synaptic mechanism underlying long-lasting changes in the excitability of pyramidal tract neurones in the anaesthetized cat. Proceedings of a Conference on "Conditioning: Representation of Involved Neural Function" Pacific Grove, California USA. Oct. 25-27, 1981. To be published, Plenum Publishing Corporation, N.Y. Ed. C.D. Woody.

#### BOOKS

\* BINDMAN, L.J. & LIPPOLD, O.C.J. (1981) The Neurophysiology of the Cerebral Cortex. publ. Edward Arnold, London. pp495.

BINDMAN, L.J., JEWELL, B.R. & SMAJE, L.H. (1978) Multiple Choice Questions in Physiology, with answers and explanatory comments. Publ. Edward Arnold, London.

## CURRICULUM VITA

Name: Dorwin Birt

PII Redacted

Education:

B.S., Purdue University, June 1968. Major: Psychology; minors Chemistry and Mathematics

Ph.D., Indiana University, October 1974 - Physiological Psychology.

Professional Experience:

Assistant Research Psychologist, Neuropsychiatric Institute, UCLA  
August 1982 to present

Neurophysiologist, Huntington Medical Research Institutes  
January 1982 to present

Visiting Research Associate, California Institute of Technology  
January 1982 to present

Senior Research Fellow, Division of Biology, California Institute of Technology  
1977 to 1982

Research Fellow, Division of Biology, California Institute of Technology  
1974 to 1977

Research Associate, Center for Neuroscience, Indiana University  
1973-74

Publications

Stewart, D. L., Birt, D. L. and Towns, L. C. Visual receptive field characteristics of superior colliculus neurons after cortical lesions in the rabbit. Vision Res. 13: 1965-1977 (1973).

Stewart, D. L., Towns, L. C. and Birt, D. L. Visual receptive field characteristics of posterior thalamic and pretectal neurons in the rabbit. Brain Res. 57: 43-57 (1973).

Stein, E. L. and Birt, D. L. Technique for stabilizing the presentation of auditory stimuli in the freely behaving rat. Physiol. Behav. 18: 729-730 (1977).

- Birt, D. L. Reorganization within the rabbit lateral posterior and dorsal lateral geniculate nuclei following complete or partial neonatal striatectomy. Presented at Neurosciences Convention, 1974.
- Birt, D., Nienhuis, R. and Olds, M. Effects of bilateral auditory cortex ablation on behavior and unit activity in rat inferior colliculus during differential conditioning. Soc. Neurosci. Abstr. 3: 231 (1977).
- Birt, D., Nienhuis, R. and Olds, M. Separation of associative from non-associative short latency changes in medial geniculate and inferior colliculus during differential conditioning and reversal in rats. Soc. Neurosci. Abstr. 4: 255 (1978).
- Birt, D., Nienhuis, R. and Olds, M. Separation of associative from non-associative short latency changes in medial geniculate and inferior colliculus during differential conditioning and reversal in rats. Brain Res. 167: 129-138 (1979).
- Birt, D. and Olds, M. E. Distribution and response characteristics of rat medial geniculate neurons which show associative change during differential conditioning and reversal. Soc. Neurosci. Abstr. 5: 314 (1979).
- Birt, D. and Olds, M. E. Associative change in neurons of intermediate and deep layers of superior colliculus of behaving rat during differential appetitive conditioning. Soc. Neurosci. Abstr. 6: 425 (1980).
- Birt, D. and Olds, M. E. Associative response changes in lateral midbrain tegmentum and medial geniculate during differential appetitive conditioning. J. Neurophysiol. 46: 1039-1055 (1981).
- Birt, D. Selective enhancement of acoustically evoked unit response in deep layers of superior colliculus by differential conditioning, submitted for publication (1982).
- Birt, D. and Olds, M. E. Auditory response enhancement during conditioning in behaving rats. In: Conditioning: Representation of Involved Neural Function, Plenum, New York, pp. 483-502 (1982).

## CURRICULUM VITAE

Name: John F. Brons

PII Redacted

**Current Position:** Postdoctoral Fellow, Department of Medical Psychology,  
University of Oregon Health Sciences Center, Portland, Ore.  
**Supervisors:** Drs. J.H. O'Brien and R.D. Fitzgerald

Education:

1965-1970	University of California Santa Barbara	Major: Cell Biology Degree: B.A.
1972-1973	University of California Los Angeles	Interdepartmental Neuroscience Program
1973-1978	University of California Los Angeles	Department of Anatomy Degree: Ph.D.

Teaching Experience (at UCLA):

Teaching assistant for:

Medical Histology  
Dental Gross Anatomy  
Dental Neurology

Lecturer for:

Course: Basic and Quantified  
Neurophysiology  
Chairman: J. Segundo, M.D.

Relevant Employment and Training

1970-1972	Location: California Institute of Technology, Pasadena, Calif. Position: Research Assistant Supervisor: Dr. Marianne Olds Responsibilities: Conduction of experiments on the cellular bases of appetitive conditioning and on the pharmacological basis of self-stimulating behavior.
1972-1975	Location: University of California, Los Angeles, Calif. Position: Lab Assistant Supervisor: R. Elul, M.D. Responsibilities: Preparation and conduction of experiments on cell electrophoresis, electrophysiological recordings from neural tissue culture, and experimental epilepsy in cats.

- 1975-1978      Location: Department of Anatomy, University of California,  
Los Angeles  
Graduate studies under the supervision of Dr. C.D. Woody.  
Dissertation Title:  
"Differences in the Excitability and Activity in Cortical  
Neurons After Pavlovian Conditioning, Extinction, and  
Presentation of the US Alone."
- 1978-1979      Location: Department of Psychiatry, University of California,  
Los Angeles.  
Position: Postgraduate Research Neurophysiologist  
Supervisor: Charles D. Woody, M.D.  
Studies into long term changes in neural excitability  
associated with unconditioned blink reflexes.
- 1979 - present      Location: Department of Medical Psychology, University of  
Oregon Health Sciences Center, Portland, Oregon.  
Position: Postdoctoral Fellow  
Supervisors: Drs. J.H. O'Brien and R.D. Fitzgerald  
Multiple unit studies of neural plasticity in brainstem  
sites associated with heart rate conditioning.

#### Publications:

- Brons, J.F., Woody, C.D., and Allon, N. Changes in excitability to weak-intensity extracellular electrical stimulation of units of pericruciate cortex in cats. J. Neurophysiol. 47: 377-388, 1982.
- Brons, J.F. and Woody, C.D. Long-term changes in excitability of cortical neurons after Pavlovian conditioning and extinction. J. Neurophysiol. 44: 605-615, 1980.
- Buchhalter, J.R., Brons, J.F., and Woody, C.D. Changes in cortical neuronal excitability after presentations of a compound auditory stimulus. Brain Res. 156: 162-167, 1978.
- Elul, R., Brons, J.F., and Kravitz, K. Surface charge modifications associated with proliferation and differentiation in neuroblastoma cultures. Nature 258: 616-617, 1975.

#### Abstracts:

- Brons, J.F. and Woody, C.D. Changes in responsiveness to glabella tap among neurons in the sensorimotor cortex of awake cats. Soc. Neurosci. Abstr. 5: 314, 1979.
- Brons, J.F., Buchhalter, J.R., and Woody, C.D. Decreases in excitability of cortical neurons to extracellularly delivered current after eyelink conditioning, extinction, and presentation of US alone. Soc. Neurosci. Abstr. 4: 255, 1978.
- Brons, J.F., Buchhalter, J.R., and Woody, C.D. Increases in excitability of cortical neurons to injected intracellular current after eyeblink conditioning, extinction, and presentation of US alone. Fed. Proc. 37: 252, 1978.

July 5, 1979

Name: Haing-Ja Kim

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Sex: Female

Education:

- B. S., 1967: Major; Physics: Minor; Mathematics: 1962-1967,  
Seoul National University, Korea
- 1971-1972, Special student at Korea University, Korea
- Major fields: Psychology and Biology
- 1973 (Jan.-June), Special student at Western College, Ohio,
- Major fields: Psychology and Biology
- 1973 (Sept.-Dec.), Graduate study at Bucknell University,  
Pennsylvania,
- Major field: Physiological Psychology
- M. A., 1976: Major; Psychology: 1974-1976, Northwestern University
- Major field; Neuroscience and behavior
- Ph. D., 1978: Major; Psychology: 1976-1978, Northwestern  
University, Evanston, Illinois
- Major field; Neuroscience and behavior

Dissertation topic: Histochemical fluorescence study of the substantia nigra and role of the nigrostriatal dopaminergic system in memory and motor functions.

Special Awards:

- 1973: University Scholarship, Western College & Bucknell Univ.
- 1974-1975: University Fellowship, Northwestern University
- 1975-1976: Teaching Assistantship, Northwestern University
- 1976-1977: University Fellowship, Northwestern University
- 1977-1978: Research Assistantship, Northwestern University
- 1974-1977, Summer: Research Assistantship and Walter-Dill-Scott Fellowship, Northwestern University

Professional Experience:

- 1969-1971: Teaching assistant in Introductory Physics,  
Seoul National University, Korea
- 1975-1976: Teaching assistant in Introductory Psychology and  
Elementary Statistics, Northwestern University
- 1978, August-present: Post-doctoral research; Intracellular  
recording from cortical motor neurons in cats

Name: Haing-Ja Kim

References:

- 1) Aryeh Routtenberg, Professor of Psychology and Biological Sciences, Cresap Neuroscience Laboratory, Northwestern University
- 2) J. Peter Rosenfeld, Professor of Psychology, Cresap Neuroscience Laboratory, Northwestern University
- 3) Ronald Clavier, Professor of Anatomy, School of Medicine, Northwestern University
- 4) Rebecca M. Santos, Research Associate, Department of Ophthalmology, Medical Center, University of Illinois, Chicago Campus

Publications:

- 1) Kim, H.-J. and Routtenberg, A. Retention disruption following post-trial picrotoxin injection into the substantia nigra. Brain Research, 1976, 113, 620-625.
- 2) Routtenberg, A. and Kim, H.-J. The substantia nigra and neostriatum: Substrates for memory consolidation. In: L. L. Butcher (Ed.) Cholinergic-monoaminergic interactions in the brain. Academic Press Inc., New York and San Francisco, 1978.

Papers presented at Neuroscience Meetings:

- 1) Kim, H.-J., Miskit, D., and Routtenberg, A. Retention impairment of passive avoidance by post-trial injection of picrotoxin into the substantia nigra in rats. Neuroscience Abstracts, 1975, Vol. 1, pp 379.
- 2) Kim, H.-J. and Routtenberg, A. Retention deficit following post-trial dopamine injection into rat neostriatum. Neuroscience Abstracts, 1976, Vol. 2, pp 445.
- 3) Kim, H.-J. and Routtenberg, A. Fluorescence microscopic mapping of substantia nigra dopamine somata and their dendrites: Relation to dopamine and non-dopamine thionin-stained cells in identical Vibratome sections. Neuroscience Abstracts, 1978, Vol. 4, pp 275.

Papers submitted for publication:

- 1) Kim, H.-J. and Routtenberg, A. The cytoarchitecture of the rat substantia nigra: Catecholamine fluorescence and Nissl-staining of identical Vibratome sections.
- 2) Kim, H.-J. and Routtenberg, A. Circling and turning induced by unilateral injection of dopamine, GHBA, picrotoxin, or kainic acid into the rat substantia nigra.

## CURRICULUM VITAE

Name: Michikazu Matsumura

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Present Address: Kyoto University  
Primate Research Institute  
Inuyama City, Aichi 484 JAPAN

Education

1969.4	Department of Biophysics	Major: Molecular Physiology
- 1973.3	Kyoto University	Degree: B. A.
1973.4	Primate Res. Inst.	Neurophysiology
- 1975.3	Kyoto University	Degree: Master
1975.4	Primate Res. Inst.	Neurophysiology
- 1978.3	Kyoto University	Degree: Ph. D.

Scholarship and Relevant Employment

1973 - 1974	Scholarship from Japanese Government
	Location: Primate Res. Inst., Kyoto University
	Supervisor: K. Kubota, M.D.
	Responsibilities: Unit and field potential recording from monkey prefrontal cortex in awake and in anesthetized state.
1975	Inter-University Exchange Program
	Location: Dept. Biological Engineering, Osaka University
	Supervisor: N. Tsukahara, M.D.
	Responsibilities: Intracellular studies in cat red nucleus and reticular formation after an ablation of cerebellar nuclei.



1976 - 1977    Scholarship from Japanese Government

**Location:** Primate Res. Inst., Kyoto University

Supervisor: K. Kubota,

**Responsibilities:** Intracellular recording from monkey motor cortex during voluntary movement.  
( Doctoral Thesis )

1978: Post-Doctoral Fellow

**Location:** Primate Res. Inst., Kyoto University

Supervisor: K. Kubota

**Responsibilities:** Histological studies of cortico-cortical afferents to hand area of monkey motor cortex with horseradish peroxidase.

**1978 - present**

Assistant Research Neurobiologist

Location: Neuropsychiatric Inst., UCLA

Supervisor: C.D. Woody, M.D.

**Responsibilities:** Intracellular investigation of excitability changes in facial motoneurons in conditioned cat.

## Publications ( papers )

Matsumura, M.

Intracellular synaptic potentials of primate motor cortex neurons during voluntary movement.

Brain Research 163, ( 1979 ) 33 - 48

Matsumura, M. and Kubota, K.

Cortical projection to hand-area from post-arcuate area in Macaque monkeys:  
a histological study of retrograde transport of horseradish peroxidase.

Neuroscience Letters 11, ( 1979 ) 241 - 246

# Abstracts

Matsumura, M. and Kubota, K.

( in Japanese ) Visual evoked potentials of monkey prefrontal cortex:  
projection pathways from visual cortex.

J. physiol. Soc. Japan 38 ( 1976 )

Matsumura, M. and Kubota, K.

Intracellular synaptic potentials of monkey motor cortex during visually-  
guided voluntary movement.

J. physiol. Soc. Japan 39 ( 1977 ) 347

Matsumura, M. and Kubota, K.

( in Japanese ) PSP activities of monkey PT neurons preceding voluntary  
hand movement.

Official Report of 2nd Annual Meeting of Visual and Chemical Perception  
( 1977 )

Matsumura, M. and Kubota, K.

( in Japanese ) Membrane properties of PT neurons in un-anesthetized  
Monkeys. Official Report of 3rd Annual Meeting of Visual and Chemical  
Perception. ( 1978 )

Iwasaki, T., Matsumura, M. and Kubota, K.

( in Japanese ) Unit activities of post arcuate neurons during Visual  
tracking task and their projections onto hand motor area.

J. EEG and EMG Japan ( 1978 )

CURRICULUM VITAE

Name: Hiroko Sakai

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Education:

1970 - B.A. International Christian University  
1972 - M.A. International Christian University  
Ph.D.

Positions Held:

1974 - 1976 Assistant Research Microbiologist  
Institute for Developmental Research  
Aichi, Japan

1976 - 1979 Assistant Research Microbiologist  
Laboratory of Neurophysiology  
Mental Retardation Research Center  
UCLA

Pre-Doctoral Fellow

Publications:

Kazuo Hara, Mimoto Hiroko, Masabumi Tanaka. Interocular transfer of visual discrimination learning sets by rhesus monkey. Annual report of the Primate Research Institute, Kyoto University 4: 45. 1974.

Yoshitaka Tamamaki and Hiroko Sakai. Stability of the responses in the Sidiman avoidance learning. Annual report of the Institute for Developmental Research 4: 36. 1975.

Hiroko Sakai and Shigehiro Kiyono. The effect of intracortical microstimulation in VL of rats. Annual Report of the Institute for Developmental Research 4: 38-39. 1975.

Yoshitaka Tamaki and Hiroko Sakai. Avoidance learning in Gunna rat. Annual report of Animal Psychology 25: 161. 1975.

## CURRICULUM VITAE

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Degrees: 1969 Bachelor of Arts: Developmental Biology, Kyoto Univ.  
 1971 Master of Science: Neurophysiology  
 1974 Doctor of Science: RIGAKUHAKUSHI (Eq. to Ph.D)

Position: 1974 Instructor of Neurophysiology  
 Primate Research Institute, Kyoto Univ.

Publications:

- Sakai, M., Niki, H., and Kubota, K., Simple monkey chair for neurophysiological studies. Advances in Neurological Sciences, 14, 164-166 (1970) (In Japanese)
- Kubota, K., Niki, H., and Sakai, M., Neurons of caudate and thalamic dorsomedial nuclei and delayed alternation performance in the rhesus monkey. J. Physiol. Soc. Japan, 33 p499 (1971)
- Niki, H., Sakai, M., and Kubota, K., Delayed alternation performance and unit activity of the caudate head and medial orbitofrontal gyrus in the monkey. Brain Research, 38, 343-353 (1972)
- Sakai, M., and Forvath, F., Unit activity of the prefrontal cortex and light-lever press reaction. J. Physiol. Soc. Japan, 35, p514 (1973)
- Sakai, M., Prefrontal unit activity during visually guided lever pressing reaction in the monkey. Brain Research, 81, 297-309 (1974)
- Sasaki, K., Kawaguchi, S., Oka, H., Sakai, M., and Mizuno, M., Electrophysiological studies on the cerebellocerebral projections in monkeys. Exp. Brain Research 24, 495-507 (1976)
- Sakai, M., Unit activity in area 6 and the isometric voluntary contraction in rhesus monkeys. Ann. Meeting Jap. Physiol. Soc. (June 1976 Sendai)

Excerpted from : Memory, Learning, and Higher Function by Charles D. Woody  
Springer-Verlag, New York, 1982.

## Chapter 7

### Cybernetics: A Means for Analysis of Neural Networks

*The development of the statistical theory of communication is a landmark in the history of communication theory. Our primary concern in a communication or control problem is the flow of messages. Since the central idea in the statistical theory is that messages and noise should be considered as random phenomena, the theory incorporates probability theory and generalized harmonic analysis in its foundation.*

(Y. W. Lee, 1960)

Commonsense approaches to an understanding of "higher function" are useful but, as we have seen, are basically introspective. Such approaches could be ill advised if used analytically because of their intrinsic susceptibility to errors, particularly those of the type illustrated in Fig. 6.6. Other, more objective means must be found to analyze the complex integrative functions of neural networks. As our knowledge of anatomically and physiologically based memory and learning advances, so must our expression of this knowledge. The form of this improved expression is likely to be mathematical and as specific as expression of our modern knowledge of genetics and the genetic codes. The purpose of this chapter is to explore some of the forms that are likely to serve for expression of our knowledge of memory and learning.

Analysis of large populations of neurons can, in principle, be approached from the same standpoint as analysis of numerically small reflex networks. The analysis requires application of systems approaches from engineering disciplines plus consideration of the limiting physiologic constraints that apply to each system analyzed. In addition, since large populations of neurons deal substantially with the processing of information, their overall analysis requires concepts from information theory.

This concluding chapter examines possible means for analyzing complex systems using mathematics, engineering, and physics. The approach is called systems analysis, but when applied to adaptive systems, it is more properly

termed cybernetics, the analytic science that deals with the control of information processing in man and machine. By using the techniques described herein, a rigorous analysis can be made of *linear* information processing systems and, perhaps, of some nonlinear systems as well [582,583,1086]. Some reflexes within the brain can be assumed to behave as a linear system and can be investigated by linear systems analysis [429,1123]. Such an analysis, though properly applicable only to theoretical systems meeting strict statistical criteria, still provides the most useful beginning toward a rigorous analysis of complex nerve networks. It simplifies the complexities of the networks, leads to formulations of the transforms of given inputs into particular outputs, and generates more precise transforms than those presently existing.

A few suitable *models* of information transfer in the brain have been developed that are amenable to mathematical analysis [cf. 18-22,366,838-841, 883,1033-1038]. The most elegant of these deals with image recognition, i.e. the transmission and processing of sensory labeled messages arising at the receptors. Minsky and Papert [672] have transformed certain problems of image recognition into problems of geometry—a transformation that elegantly simplifies many problems of analysis. Then, they have devised a theorem, the Group Invariance Theorem, that provides a general analytic solution for one set of the geometry. In application, the Group Invariance Theorem (p. 388) adequately describes the geometry of sensory reception for the components of two specific models of elements of an image recognition network, the perceptron and the informon. In these models, as in the brain itself, line labeling appears to be the key to following the flow of information through its complex transformation from sensory input into motor output. Flowgraphs and linear systems analysis are also helpful in this regard.

Each of these analytic approaches properly begins by considering known constraints on the system to be analyzed. Therefore, before discussing the models and their analysis, some constraints on information processing that any useful model of brain function should satisfy will be considered.

## Constraints

### Time Constants of Neural Information Flow

How rapidly can information be transmitted and processed within the CNS?

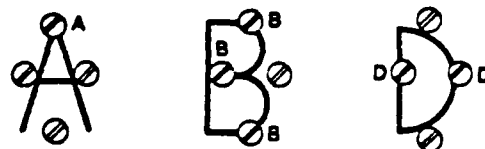
#### *Conduction Time and Transmission Delay*

As noted earlier in Chapter 2, the rate of nerve conduction is a function of fiber size, with large axons conducting more rapidly than small axons. Transmission of an electrically propagated impulse along a neuron may proceed as rapidly as 160 m/sec in the dorsal spinocerebellar tract of the cat [369] or as slowly as 0.5 m/sec in the finest, unmyelinated axons of the spinothalamic system [693]. Thus, while it could take as little as 2 msec for proprioceptive information concerning hindleg position to reach the cerebellum of the cat (a distance of about 320 mm), it could take as long as 640 msec for infor-

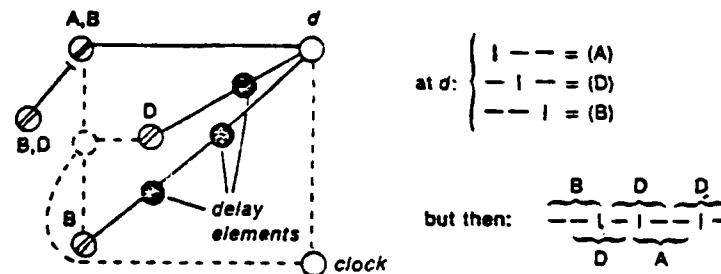
\* \* \* \* \*

# Automata Design

## I. Receptors



## II. Spatial signal-serial processor-temporal code



## III. Spatial signal-parallel processor-Spatial code

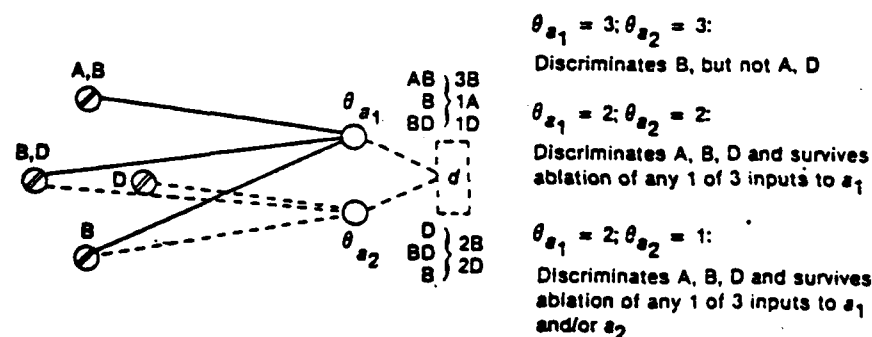
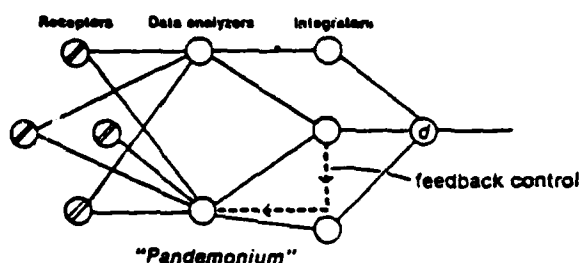
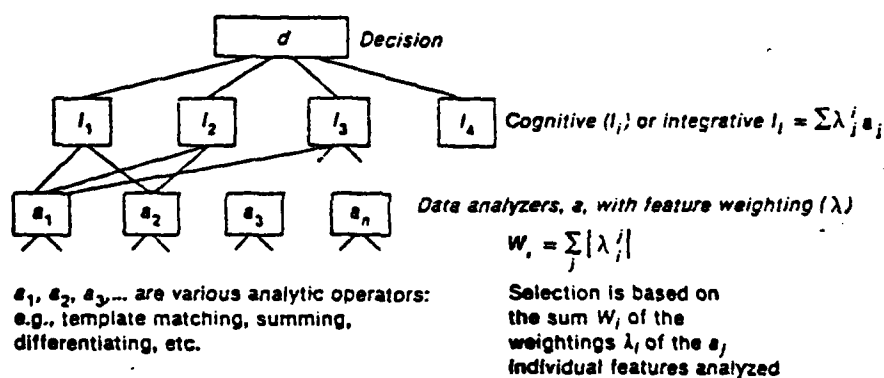


Fig. 7.5. Examples of the components of different automata. I. Receptor elements common to each example. The uppermost of the four elements is receptive to (and intersected by) the letters A and B but not D. The lowest element is receptive to B only. The receptivity of the remaining two elements is as indicated. II-IV. Automata with different network architectures: II, serial time dependent, III, parallel perceptron, IV, parallel pandemonium. In II three

## IV. Feature weighting and analysis plus feedback control



## V. Feature detection and evolution



different coded outputs of the decisional element,  $d$ , are shown to the right. Below, the ambiguity of this coding is illustrated when its beginning in time is uncertain. In III changing  $\theta$ , the number of inputs required to fire the second order elements, changes the discriminative property of the network as discussed in the text and summarized in the diagram to the right. In IV a variation on III introduces feature detection (e.g., summation, filtering, etc.) as well as feedback control (heavy dashed line) into the circuit. A version of IV is shown below (V) in which details have been inserted after Selfridge's pandemonium [883]. Selection of evaluation of the individual demons for permutation is based on  $W_i$ , the sum of the weightings,  $\lambda_i$ , of the individual feature detectors,  $a_i$ .

The filled circles represent serial time delay elements. The elements comprised by dashed lines represent a clocking mechanism that keeps track of time following presentation of the stimulus pattern at the receptors. Depending on which receptor is activated, a time coded signal 1-, -1-, or -1 will be generated at the decision-making element,  $d$ . Note that if track



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is not kept of time (see Fig. 7.5, II, lower right), the code becomes ambiguous. Though the example is oversimplified, it is quite representative of the type of processing that is widely used in digital computers.

The term parallel processing was originally used to designate performance of the same processing operation by more than one channel at a time. The purpose was to support majority logic and redundant signal processing as discussed earlier. *Multiplexed*, parallel processing resembles much of the processing done by the brain. In the example shown in Fig. 7.5, III, the second-order elements receive redundant messages and parallel processing is used to generate a "decisional" output at element "d". As can be seen, this type of processing has remarkable sorting or discriminative properties when adaptation is introduced.

If each of the second order elements in Fig. 7.5 III is set to fire when three inputs are received (3/3), the network will distinguish B, but not A from D, i.e.,  $a_1$  (fires) = B. If the "threshold" is reduced to discharge upon reception of two inputs (2/2), the network will then discriminate A, B, and D. An A will be designated by no discharge, a B by discharge of both elements, and a D by discharge of the lower element, i.e.,  $\bar{a}_1 \bar{a}_2 = A$  (or nothing presented),  $a_1 a_2 = B$ ,  $\bar{a}_1 a_2 = D$ . Moreover, the network will continue to function despite destruction of any one of the three input lines to the upper element.

Although one must beware of making exact transpositions between mechanical and physiologic models, many of the same, general theoretical considerations concerning learning, memory, and even higher function apply to machines as to physiologic systems. The machines give us a physical model which is more accessible to analysis and is more easily studied. Three machine automata stand out from the others in providing insightful models of learning operations, component interactions, and the constraints thereof. They are the perceptron, pandemonium, and the informon.

### Perceptron

The perceptron represents an early attempt by Rosenblatt and colleagues to develop a learning automaton based on their conceptions of brain organization [838-841]. In this device, the components consist simply of modifiable elements and their interconnections. As shown in Fig. 7.26,  $\alpha$  is the sum of the components  $\psi(x)$ , each weighted by  $\alpha_\psi$ . When the weightings are modified ( $\Delta\alpha$ ), the system can adapt to distinguish a particular input, identified when  $\psi$  is  $\geq$  some predetermined value,  $\theta$ .

$$\psi = \sum \alpha_\psi \psi(x) \geq \theta, \quad (7.2)$$

where  $\Delta\alpha$  reflects adaptation.

The example of parallel processing (Fig. 7.5, III) can be viewed as a perceptron by making  $d = \sum$  and considering  $a_1$  and  $a_2$  as having weighted inputs depending on the threshold settings,  $\theta_a$ .

In such systems, the performance of pattern recognition can be adaptively improved with relatively simple algorithms of element modification as illustrated in Fig. 7.5 (additional algorithms are listed on p. 395). Although this can be done among elements with randomly organized connections, as the original perceptron demonstrated, a more efficient operation will be provided by a nonrandomly organized network. Thus, the organization of the adaptive network may become a critical variable in the learning operations that are performed by such a system.

#### Pandemonium

An example of a nonrandomly organized automaton is *pandemonium* of Oliver Selfridge [883]. Its organization is hierarchical, being characterized by multiple layers supporting different operations as shown in Fig. 7.5, IV and V. The initial layer again consists of simple receptor or data collecting elements, termed data demons by Selfridge. The second layer consists of specialized analyzers or computational demons. They process incoming data by stereotyped procedures such as matched filtering, summation, or differentiation. The third layer consists of integrators or cognitive demons. They integrate weighted inputs from various computational demons. Finally, a decision maker or "decision demon" selects the loudest or most active cognitive demon(s) and by its (their) identity gives priority to a selected set of receptors.

Within this hierarchy, adaptation occurs according to rules of reinforcement specified in terms of the effectiveness of each element in performing the selected recognition task. Elements which are more contributory to successful image recognition are positively reinforced by increasing their weighting. Elements which are less contributory are eliminated. Permutations of the analytic algorithms of successful elements are generated to replace those of unsuccessful elements. Hill-climbing techniques are used to secure continued improvements of the adaptations with extensive attention paid to the problem of avoiding false peaks.

Several insights into adaptive information processing are provided by pandemonium. Pandemonium is characterized as a chaotic operation with demons, subdemons, and sub-subdemons shrieking their outputs, adapting, deciding, and sometimes evolving. However, the chaos turns out to be more orderly than expected. All the analytic functions are particularized and are, to a significant degree, predetermined. Despite the great degree of adaptability within the hierarchy, the hierarchy is relatively fixed. The reason for this is that, although the adaptability permits evolution, it is along a predictable pathway, and occurs within a particular hierarchy. (This feature appears to have led this particular automata to a particularly tenacious pursuit of false peaks during hill-climbing adaptive operations.) Differences in the design of the hierarchy selected for Pandemonium versus that shown in Fig. 3.42 may therefore be of some consequence. The ability to switch between elements may need to be matched by an ability to switch between hierarchies.

**Informon**

The *informon* model of Uttley [1033-1038] takes a somewhat different approach to the design of an automaton, concentrating on improving the construction of the fundamental adaptive element itself. The basic informon consists of a single element with multiple inputs  $F(x_n)$  and an output (Fig. 7.6). The inputs have variable weightings,  $\alpha$ . One of the inputs is defined as a reinforcing input  $F(z)$  with a fixed negative weighting,  $-k$ . There is also provision for negative feedback of information concerning the operational state of the element,  $F(Y)$ . The negative feedback is required for stability of the adaptive process.  $F(Y)$  is some function of the output of the element prior to the state of binary, spike discharge. There is finally a threshold device,  $\theta$ , at or just before the output, which can be used to discriminate between different sets of inputs.

Several additional variables (or constraints) are required for the informon to discriminate successfully one particular input  $F(x_i)$  from another,  $F(x_{ii})$ . These are:

1. The algorithm by which  $\alpha_i$  is altered ( $\Delta \alpha$ ).
2. The need for a reinforcing input,  $F(z)$ , to distinguish or identify which input signal is the particular signal to be discriminated.
3. The need to achieve some system normalization through negative (not positive) feedback of information regarding the current system state,  $F(Y)$ .

Note also that by picking the adaptive algorithm correctly (e.g., log of the mutual information between inputs), one can greatly facilitate both normalization and input discrimination.

**Algorithm for  $\Delta \alpha$** 

The trick here is to choose an algorithm that will produce S-shaped adaptive operations such as are found with conditioning or other simple forms of learning. It will also be useful to have a decay or extinction phase of adaptation. Adaptation is performed by changing the weighting,  $\alpha$ , of an input.

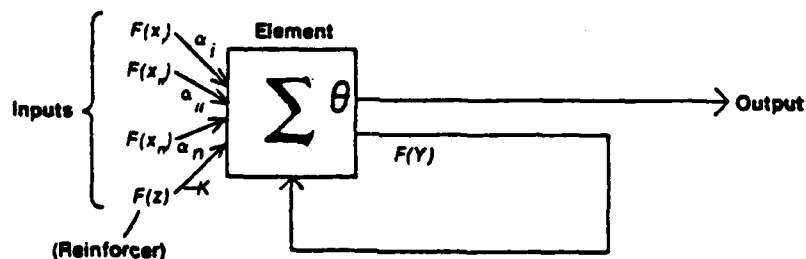
**Simple Informon**

Fig. 7.6. The basic informon element. See text for further details. (After Uttley [1038].)

Figure 7.7 shows such an operation graphically and enables us to see how a particular choice of algorithm may or may not produce a stable change in weighting.

Uttley points out that analysis in the phase plane between change in  $\alpha$  (i.e.,  $\Delta\alpha$ ) and  $\alpha$  itself reveals the limitations of certain algorithms, notably those proposed by Hebb [397] and by Brindley [97] and Marr [646]. This is shown in Fig. 7.8.

Hebb's postulate that an input causes an increased output simply indicates that if  $\alpha$  is positive so must be  $\Delta\alpha$ . This postulate places the algorithm for acquisition within the right upper quadrant (++) of Fig. 7.8, but fails to specify a relationship or slope between variables  $\Delta\alpha$  and  $\alpha$ . Brindley [97] and Marr [646], in effect, consider a pathway with two states, one initial and one final, in which  $\Delta\alpha$  and  $\alpha$  increase together. With limiting values this reduces to an all-or-none, two state process. Without limiting values this represents an unstable system with positive feedback which will lead to regenerative explosion (line "a" in Fig. 7.8).<sup>\*</sup> Uttley picks an algorithm which allows the values of  $\Delta\alpha$  and  $\alpha$  to fluctuate in the manner shown by lines "b" and "c" of Fig. 7.8 [1036].

#### *System Normalization by Feedback of System State*

Uttley points out that regenerative explosion may be avoided by introducing a normalization process, such as that of Malsburg [1047]. However, Malsburg's type of normalization shows an overly restrictive range of successful

#### *Adaptation in an Informon*

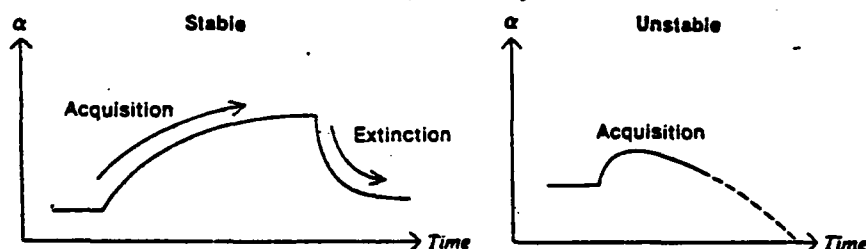


Fig. 7.7. Adaptation in an informon involves changes in  $\alpha$ , the weightings of input, over time. In the example to the left an increase in  $\alpha$  occurs during acquisition of input facilitation and a decrease occurs during its extinction or defacilitation. The parallel between this and conditioned behavior is deliberate. In the example to the right acquisition is an unstable process with  $\alpha$  declining unintentionally past a certain transition point. This may occur because of failure to regulate the system state appropriately during the adaptive process. See text for further details about regulating the system state (After Uttley [1036].)

<sup>\*</sup>This problem is avoided in some nonlinear systems that change state as levels reach certain limits.

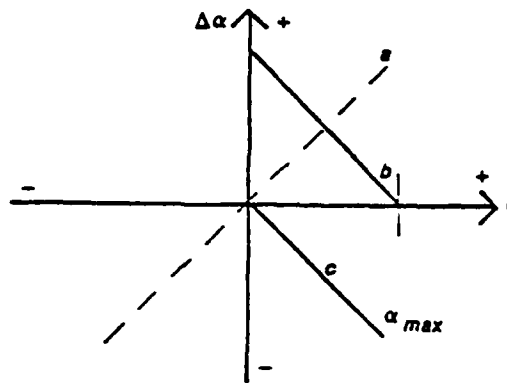
Phase Plane Between  $\Delta\alpha$  and  $\alpha$ 

Fig. 7.8. Phase plane of  $\alpha$  versus change in  $\alpha$  (i.e.,  $\Delta\alpha$ ). State changes along "a" such as those proposed by Marr [646] and Brindley [97] are unstable, while those along "b" or "c" are not. b mirrors the state change during acquisition in Fig. 7.7; "c" mirrors the state change during extinction. (After Uttley [1036].)

operation when applied to a system with positive feedback. To avoid this, Uttley turns to negative feedback as shown in Eq. 7.3b. Thus, the adaptation of his element, and probably some neuronal elements as well, depends critically on negative feedback of information concerning the system state,  $F(Y)$ . Normalization results in part from the negative feedback of information concerning the system state (Fig. 7.9) and in part from the choice of adaptive algorithms described below (Eqs. 7.3a, 7.3b, and 7.5).

$$\Delta\alpha_i = -kF(x_i)F(Y), \quad (7.3a)$$

where  $F(Y) = \sum F(x_i)/\alpha_i$  and  $k$  is a positive constant.

However, this is still not enough to permit successful input discrimination, which depends additionally upon introduction of a reinforcing input.

**Reinforcing Input**

Reinforcement, or identification of the particular input  $F(x_i)$  to be discriminated or enhanced by increasing  $\alpha_i$ , is done by introducing a separate, labeling input  $F(z)$  with  $\alpha_z$  fixed and negative (Eq. 7.3b).

$$\Delta\alpha_i = -kF(x_i) [\sum F(x_i) \alpha_i + F(z) \alpha_z] \quad (7.3b)$$

Given an input  $F(x_i)$ ,  $\alpha_i$  will increase if  $F(z)$  is present and will decrease if  $F(z)$  is absent. With repeated reinforcement,  $\alpha_i$  assumes the function of the acquisition curve shown in Fig. 7.7 (left) with  $\Delta\alpha_i = \alpha_{\max} - \alpha_i$  (line "b" of

**Significance of Locus of Negative Feedback of Information Concerning System State Relative to Level at which the System State Becomes a Binary, All-or-None Output**

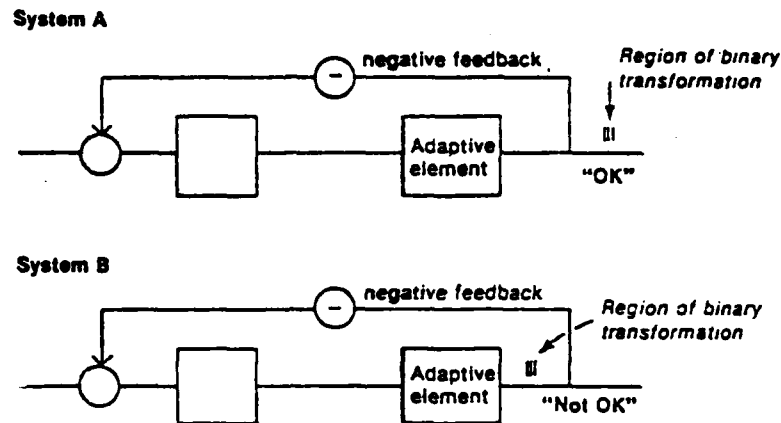


Fig. 7.9. By changing the locus of negative feedback so that instead of sampling the internal state of the adaptive element, as in (A), one samples only the binary output of the adaptive element, as in (B), one loses information required for normalization and an unsatisfactory adaptive process may ensue. The location of the binary encoder is shown by ||| (Cf. Uttley [1033].)

Fig. 7.8). Without reinforcement,  $\alpha_i$  assumes the function of the extinction curve in Fig. 7.7 (left), with  $\Delta\alpha_i = \alpha_i$  (line "c" of Fig. 7.8). Without a reinforcer,  $F(z)$ , a curve such as that shown in Fig. 7.7 (right) would be obtained.

The transfer properties of Uttley's adaptive element are designed then to simulate the S-shaped acquisition curve of conditioning plus its decrement during extinction. Considerable attention is also paid to controlling and limiting elemental adaptation by closed loop, negative feedback of the element's internal state. This variable provides a significant constraint on the operation of the adaptive element and may constitute a general requirement of successful self-organizing adaptive operations.

**Mutual Information Constraint**

Uttley imposes one further constraint on the operation of an informon, namely, that  $\alpha$  be a modification of Shannon's mutual information function\*:

$$\log \frac{P(x_i \text{ and } Y)}{P(x_i)P(Y)} = I(x_i; Y)$$

\*see p. 381

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This constraint can be applied to the operation specified in Eq. 7.3b. As a result:

$$\alpha_i = K[\ln F(x_i) + \ln F(Y) - \ln F(x_i)F(Y)]^* \quad (7.4)$$

or to simplify

$$\alpha_i = -KI(x_i:Y) \quad (7.5)$$

Thus, an increase in  $F(x_i)$  will result in an increase in  $\alpha_i$ ; an increase in  $F(Y)$  will also increase  $\alpha_i$ , but an increase in  $F(x_i)F(Y)$  will decrease  $\alpha_i$ .<sup>†</sup>

In summary, parallel processing systems with adaptive elements appear to handle discrimination tasks quite easily. Hierarchically organized networks, such as pandemonium, with non-uniform elements and specialized adaptive properties can handle some forms of learning with particular ease, but may cling tenaciously to errors in discrimination arising from their particular design. (This erroneous "behavior" is not unlike that of perseveration and neglect described in Chapter 6.) Other automata, such as the informon, may rely on optimized properties of more uniform adaptive elements. As Uttley has shown [1036-1038], the adaptive weightings must change in ways that are nonexplosive. Introduction of negative feedback of information concerning the state of the controlled system can contribute to a normalization process which, in turn, can reduce the possibility of explosive change. Other features such as relaxation of increased weighting and discriminative control of the weighting changes of certain inputs require additional features. These may include particularized dependencies between inputs such as the mutual information feature of Uttley's model or labeled reinforcing inputs such as  $F(z)$  of Uttley's model.<sup>‡</sup>

By slightly redefining Uttley's circuits (Fig. 7.10), it is possible to form closed loop, positive feedback pathways that might support motor labeling in classical, associative conditioning (see Chapter 3). Positive feedback would augment a particular message of motor significance transmitted within a specific, closed loop circuit. The augmented message would facilitate the formation of adaptations along the pathway. Another mechanism (e.g. inactivation) would be required to avoid explosive change.

Further support for a possible role of positive feedback in neural control systems is furnished by Freeman's model of olfactory bulb circuitry [299]. In that model, the effect of the stimulus is to increase feedback gain in an ensemble of neurons that are receptive to the stimulus. "If a local ensemble containing sensitized subsets that are mutually excitatory is excited, the basis exists for a regenerative increase in activity in response to an adequate stimulus" [299]. The model has five main features:

\*a simplification; properly, the equation incorporates the ensemble average of the frequencies of signal occurrence. See Uttley [1036].

†Further material concerning these equations can be found on pp. 381,382.

‡For further particularizations of interest, see Uttley, A. M. *Information Transmission in the Nervous System*. London: Academic Press, 1979.

## Feedback of Motor Labeled Information

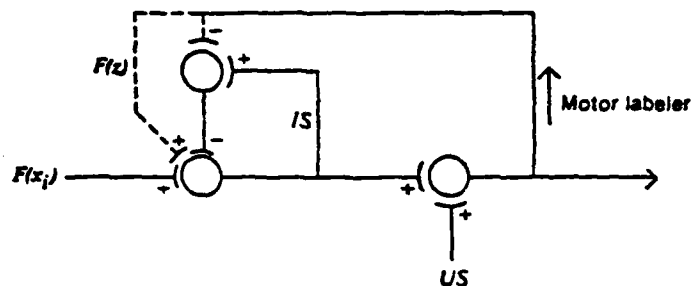


Fig. 7.10. Schema for motor (M) labeled reinforcements derived from Uttley's informon model. The US activates neurons which act directly (or indirectly) as the  $F(z)$  input. Selective labeling of the "upstream" neurons which project, selectively, to the activated units is potentiated because of positive feedback within the circuitry. For this schema to operate successfully, some feature such as local recurrent inhibition would be required to monitor the system state and prevent explosive buildup from the positive feedback. IS=feedback of information concerning internal system state.

1. A nonlinear signal range that is near linear about the origin.
2. Bilateral saturation with gain approaching zero at both extremes of wave amplitude (this feature provides stability).
3. A 2:1 asymmetry of the asymptotes of the circuit transfer function (arising from the features of the olfactory bulb and cortical electrophysiology on which the system is modeled).
4. A gain that increases with positive (excitatory) input.
5. A gain that is modifiable in a pattern that depends on background or steady state activity, which in turn is presumed to be under centrifugal control.

The positive feedback should satisfy three constraints for stability: (1) the regenerative effect should not be unduly perturbed by noise, (2) it should be self-limiting in maximal amplitude, and (3) it should be rapidly self-terminating to permit additional inputs to pass [299].

## Analysis

Analysis of the organization of systems as complex as the brain need not be considered impossible when systems involving complex communication (television), learning (computer automata), elaborate control mechanisms (guided missiles), and even uncertainty (the atom) have proved amenable to analysis. It is possible, in principle, to analyze a complex system if it is finite, obeys the laws of physics, and meets the constraints of the analytic method.\* This

\*One should never underestimate the importance of this latter consideration (see pp. 322-401 and Epilogue).



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is so irrespective of whether the system is biological or mechanical. Means exist, such as linear systems analysis (p. 366), for partitioning many complex systems into relevant suboperations that are easier to analyze, and some neural systems are amenable to this form of partitioning [429,1103,1123]. Other means such as flow graph techniques (p. 368) can be used to analyze neural network operations on a cell to cell basis despite complex interrelationships including feedback between receptor and effector functions. Finally, means can be found, as by computer simulations, to reassemble and test the analyzed component functions with reference to the overall organization of the network.

Apart from complexity, another objection that is frequently raised to analyzing brain function is that general physical theories comparable to those found in chemistry or other basic disciplines are lacking. While it is true that theories of information handling are not so advanced as those in other fields, the existing theories have been found applicable to predictive treatment of information handling by real systems. The usefulness of Shannon's information coding theories in the communications industry is well established and has been complemented by the emergence of additional theories in the areas of systems control. The challenge for neuroscientists is to develop extensions of the above theories that are applicable to treatment of specific neural information processing systems. The basic purpose of the material that follows is less ambitious, being simply to outline some of the potentially relevant analytic methodologies.

## Signal Analysis

The fundamental idea of Wiener and Lee's approach to analysis of communications systems is that messages, signals, and noise should be considered statistically and described in terms of probability theory [582]. Messages are information carrying functions, i.e. member functions in an ensemble, or numerically large aggregate, of signals (relevant information) and noise (irrelevant information) and their combination. Communication theory has led to analysis of linear message-transmission systems using convolution as the basic analytic device. Given a linear system (p. 396) and consideration of signals and noise as random processes [582], signal analysis can be performed by time series analysis utilizing (1) Fourier series, (2) power spectral density, (3) correlation, and (4) convolution (Table 7.2).

Most signals to be analyzed within the CNS are changes in voltage or current as a function of time. To determine the structure of a signal, it is analyzed in terms of its frequency components (c.f. Figs. 5.30, 7.11, 7.12, and 7.14). The signal may be described in terms of its major frequency components (Figs. 7.11, 7.12) or, more precisely, in terms of the power consumed across a 1 ohm resistor by passage of the different frequency components of the signal (including harmonics). The latter is called the power spectral density (Fig. 7.14). Some information, that concerning the phase of one frequency component

\* \* \* \* \*

## Control of Adaptive Systems

Linear systems analysis admits a general theory of adaptive control provided that the system is linear and the usual constraints are satisfied. One constraint is that the result of adaptation depend on the entire past history of adaptation within the system. Another is (usually) that the transfer function of the system be time invariant.

When using this theory, adaptation is introduced as a controller function,  $g(t)$ , as in Fig. 7.24. It operates by adding an additional input to the system much like  $F(Y)$ , the negative feedback of the system state, in Uttley's informon. It does not directly modify the original system transfer function,  $H(t)$ . To do the latter would lead to a time-variant or self-organizing adaptive system which could easily be nonlinear and, therefore, not amenable to analysis by this theory.

For a linear system with the feedback circuit shown in Fig. 7.24(A), the output,  $Y(t)$  is a function of the input,  $X(t)$ , the system transfer function,  $H(t)$  and the controller function,  $g(t)$ . If the Laplace transform,  $F(s)$ , of each function is taken,

$$\text{e.g., Output } F(y) = \int_0^{\infty} Y(t) e^{-st} dt, \quad (7.49)$$

(note relationship to Fourier transform, Eq. 7.6), then, for a linear system,

$$\text{where} \quad f_1 * f_2 = F_1(s) F_2(s) \quad (7.50)$$

i.e., in the absence of a control loop,

$$F(y) = F(x) F(h). \quad (7.51)$$

The output of the linear system with *negative* feedback (Fig. 7.24A) may therefore be expressed as

$$F(y) = \frac{F(h) F(x)}{1 + F(h) F(g)} \quad (7.52)$$

For the feedforward circuit shown in Fig. 7.24(B),

$$F(y) = 1 + F(g) F(x) F(h) \quad (7.53)$$

assuming *positive* feedforward.

One may wish to consider the linear control circuits of Fig. 7.24, the designs of automata shown in Fig. 7.5, and the algorithms of adaptation listed on p. 395 in relation to the descriptions of control systems that follow.

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*Control Systems*

Several types of control systems are recognized, each with its own critical feature(s). For example, there are:

Control systems:

1. With or without memory.
2. With or without set point variance.
3. With or without self-organizing adaptation.
4. With open or closed loop control.
5. With feedforward or feedback control.

The list is by no means complete or (in considering how to classify different types of switches, flywheel governors, thermostats, and innate or learned behaviors) are all of the differences unique or mutually exclusive.

Adaptations involved in control may reach some maximum or minimum value, or may proceed at some steady state level with or without range bounding as was described earlier (Figs. 7.7, 7.8).

*Open Loop Adaptive Control Systems*

An open loop control system receives no feedback information regarding the state of the adaptive system. There may be indirect feedback of information (e.g., from the environment and changes therein caused by the system's operation) to support the predetermined system operation, but not to cause the controller to adapt. Control is exercised entirely by predetermined adaptations based on the detection of predefined contingencies. Thus, in a thermostat adaptation occurs on the basis of temperature detection plus a prespecified contingency (if the temperature is low, turn on the heat; if high, turn it off). There is no feedback to alter the rules of adaptation based on past performance. There is instead an input of ambient temperature and a fixed course of adaptation contingent on its level. Neuronally, open loop adaptation may be contingent on two different synaptic inputs occurring together, as with heterosynaptic facilitation and inhibition.

Open loop control systems will typically have great stability since their adaptive features are entirely predetermined. However, it may be difficult to achieve a control operation of high sensitivity with an open loop system. This is because the accuracy of control depends on the system's initial calibration and on the precision of the involved components. The operation of open loop control systems will be vulnerable to component breakdown or interference from outside noise that was unanticipated in their original control design. Driftage away from the initial component set point is uncorrectable with an open loop control system. There is also no possibility for self-organizing adaptation, since there is no regard for the present or past system state.

*Closed Loop, Feedback Control Systems*

A closed loop control system normally uses feedback concerning the value of a controlled variable or the state of the adaptive control system, as a means to control further adaptation. In a closed loop, self-organizing control system, the response of the modified element should have a direct effect on the

control action (Fig. 7.24A). This circuit may be compared with that of a feed-forward control system (Fig. 7.24B) in which information from the input modifies the controller without regard to the system state.

Either feedback or feedforward circuitry can be used to reduce the error or improve the response time of linear control operations, such as described earlier, and the circuitries may be either positive or negative. Because of the closed loop operation, feedback may have self-potentiating effects when it operates either as a supplemental control input to the system or as a self-organizing modifier of the system's original transfer function. Positive (regenerative) feedback is distinguished from negative (degenerative) feedback in that the former augments the gain of the loop system and can lead to explosive buildup. *Positive feedback* returns an output to the input so as to add another, positive input. This will permit rapid change or increased sensitivity of the system by which transforms between input and output are performed; however, it also tends to unstabilize the system and increase distortion of the signal input. *Negative feedback* returns the output to the input in such a way as to add another, negative input. Negative feedback then decreases the gain of the loop system and can lead to damping or a cut off of signal transmission. This tends to stabilize the transfer between input and output and reduce distortion, although the sensitivity and rapidity of the transfer operation may be reduced.

Negative feedback control systems have a system response that is relatively insensitive to brief external disturbances and to internal variations in parameters of the operations controlled. This is because the output, e.g.,  $F(y)$  in Eq. 7.52, approaches  $F(x) \div F(g)$  if  $F'(y) F(g) \gg 1$ . Thus, small deviations in component operations or even the original control parameters may not overly disturb the control system, provided that their manifestations are accessible to the control loop. This permits relatively noisy components to be used for the system operation. Note, however, that when a closed loop system is

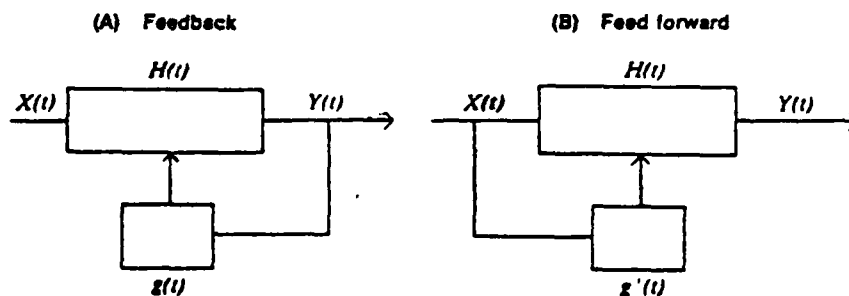


Fig. 7.24. Linear systems with feedback control (A) and feedforward control (B). The systems have input  $X(t)$ , transfer function  $H(t)$  and output  $Y(t)$ .  $g(t)$  and  $g'(t)$  are the controller functions. Differences between applying the output of the controller function as an "extra" (additive) system input versus applying it to direct adaptation of the system transfer function are discussed in the text.

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carrying a range of frequencies over the feedback path, the frequency characteristics of the network may become an important source of error. At one frequency the phase of the signal fed back may be such as to produce negative feedback, but at another frequency the phase relationships may be such as to cause positive feedback, and oscillations may occur. Stability of control can therefore be a problem with closed loop control operations, since with closed loop adaptive control, there may be oscillating errors of overcorrection leading to explosive instability or drift in an undesired direction. The latter feature, taken in a converse manner, lends itself to self-organizing adaptive control, provided that some means be found to avoid maladaptation.

Some typical characteristics of closed loop systems which may be of interest with regard to their possible use in the design of self-organizing systems are as follows:

1. Some stable closed loop systems tend to have a transient response performance which can be predicted from the steady-state, closed loop plot of magnitude versus frequency (e.g., Nyquist plot).
2. A system designed for optimal steady-state operation may have unstable transient characteristics.
3. Self-organizing adaptive systems, i.e., control systems that incorporate time-variance based on system operation into the adaptive scheme, must have some means of evaluating how well the control operations are being performed. This index of performance must be reliable and unambiguous with respect to the optimal range of operation.
4. It should be possible to obtain a performance index without disturbing the operation of the system and in a form which is amenable to insertion into that part of the system in which control of adaptation is accomplished.
5. If hill-climbing techniques are used to control steady-state adaptation [e.g., 883], false peaks must be defined and avoided.

#### Other Mathematical Techniques

The two theories that follow are introduced because of their promise for advancing our ability to analyze complex adaptive networks. Their mention is abbreviated because of their novelty and because so little is known at present about their proper application.

#### *Ergodic Theory*

Ergodic theory "is concerned with the average behavior of large collections of molecules that move randomly for indefinite periods of time . . . Ergodic theorists commonly deal with measure and probability spaces and have developed powerful theorems involving ramification of these ideas [537]." The reader is referred to Kolata [537] for further discussion of ergodic theory.

#### *Field Theory*

"Field theory, as elaborated by Weiss, Wolpert, and others," indicates that a field "can be defined operationally as a domain within which changes in the

## Specific Theories of Line Labeled Information Handling 387

presumptive fates of cells can occur" [300]. Cells may be assigned positional values according to their physical locations in the coordinate system of a particular field. In terms of positional information theory, the field can be defined as a set of cells which have their positions specified with respect to the same coordinate system. Further information is available elsewhere [300].

## Specific Theories of Line Labeled Information Handling

## A Geometry of Perception--Processing of Sensory Labeled Information

Minsky and Papert [672] have uncovered the beginnings of a powerful mathematical theory concerning a geometry of perception pertaining to the processing of sensory labeled information. The theory also deals with adaptive features of the processing. The topologic transformation of problems of image recognition and perception into problems of line labeled geometry is insightful and potentially more useful than these authors may have imagined originally.

As shown in Fig. 7.25, image processing involves sets of receptive elements that receive and process aggregates of sensory labeled information. Each unique, sensory labeled set independently processes its sensory aggregate according to some function,  $\varphi_i$ . The results of processing by each set are combined by means of a function  $\Omega$  to obtain the value,  $\psi$ . The problems to be resolved are:

1. How can arrays of this sort be organized to permit a particular  $\psi(X)$  to be a useful designator of a particular input,  $X$ , at the receptor elements?
2. Can a geometry be devised that will describe this process precisely and define some reasonably optimal approach to this problem?

Minsky and Papert begin their solution of these problems by pointing out that some meaningful restrictions must be placed on the function  $\Omega$  and the set  $\Phi$  of functions  $\varphi_1, \varphi_2, \dots, \varphi_n$  if the geometry is to be useful. And they point out that previous treatments of this type have been more anecdotal than mathematical.

It is also desirable to introduce variable weighting or some other potential means of adaptation, into the analysis. As shown in Fig. 7.26, weightings  $\alpha_1, \alpha_2, \dots, \alpha_n$  may be assigned each function  $\varphi_1, \varphi_2, \dots, \varphi_n$ .

In addition,  $\Omega$  may be replaced by a summation or integration function,  $\Sigma$ , and a threshold detector,  $\theta$ , may be added to designate a particular value or region of  $\psi$ . When  $\alpha$  is variable, this constitutes a simple perceptron, named after the automata of this general type that were designed by Rosenblatt [838-841]. It is noted by Minsky and Papert that in such automata  $\alpha$  tends to grow faster than  $\Omega$  in adaptive processing operations requiring memory storage.

The more complex perceptron admits multiple, redundant inputs as shown in Fig. 7.27. This type of processing of sensory labeled information corresponds closely to that carried out by the nervous system and is amenable to analysis by means of the Group Invariance Theorem.

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## A Simple Image-Processing Automaton

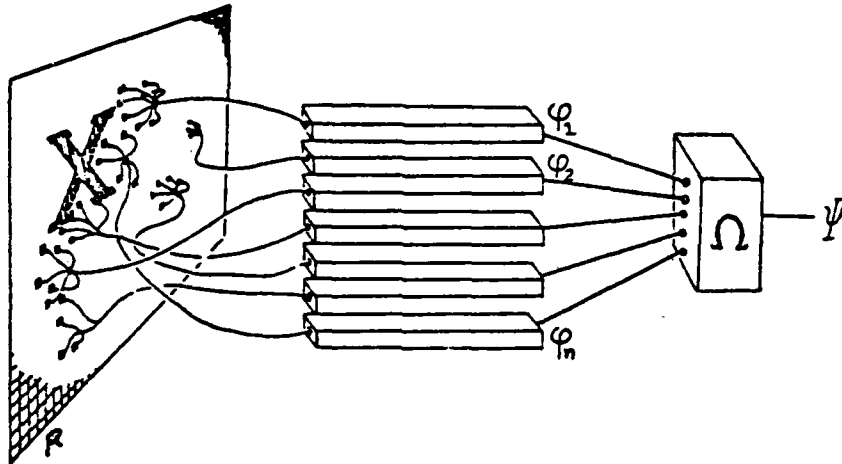


Fig. 7.25. An example of simple, multiple channel, image processing. See text for further details (From Minsky and Papert [672].)

*Group Invariance Theorem*

The Group Invariance Theorem of Minsky and Papert permits analysis of perceptron operations (i.e., the geometry of sensory image processing) by algebra instead of statistics. This theorem examines the relationship between all possible receptor activations (all sets of sensory labels,  $r_1, r_2, \dots, r_n$ ) and their representation across a theoretical space of  $\alpha_{\phi\psi}(X)$  for  $\phi \in \Phi$ .

## A Perceptron

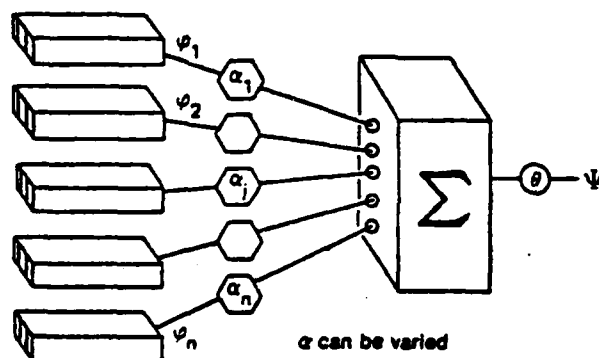


Fig. 7.26. Elementary perceptron ( $\alpha$  can be varied). (From Minsky and Papert [672].)

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Equivalence Between Parallel Processing and Group Invariance Theorem

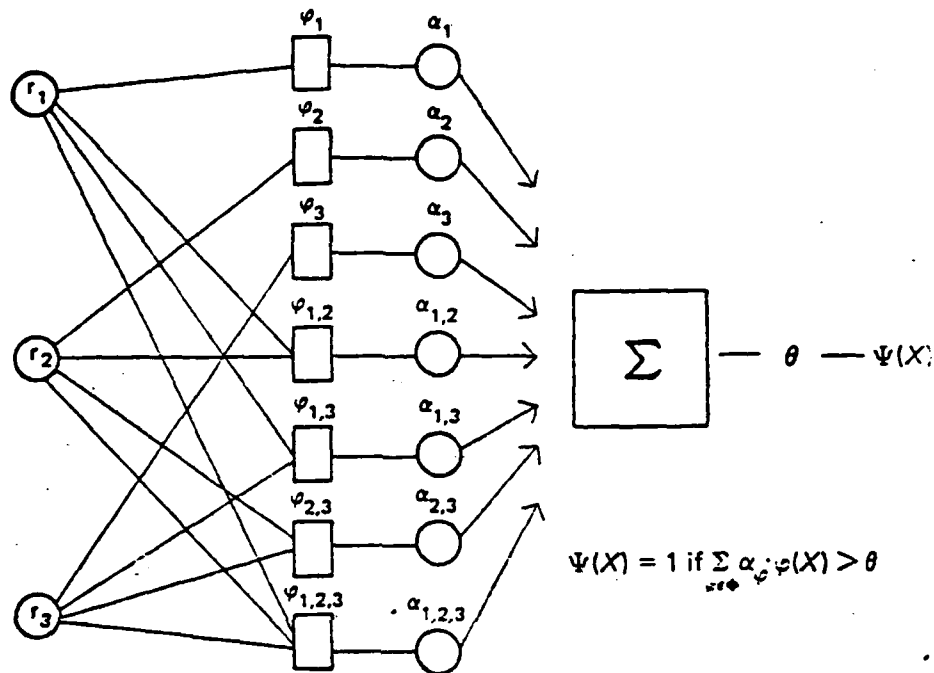


Fig. 7.27. A perceptron reduced to Group Invariance Theorem coefficients. (From Minsky and Papert [672].)

In effect, the Group Invariance Theorem permits an algebraic analysis of all geometries of rearrangements (or representations) of the original set of possible receptor labeled activations. It allows determination of which aggregates of  $\alpha_{\phi} \phi(X)$  (or values of  $\psi$ ) reflect a unique transformation of the group of possible transformations of the space of the receptor labelings,  $r_1, r_2, \dots, r_n$ , upon the predicates,  $\phi_1, \phi_2, \dots, \phi_n$ .

Given any predicate  $\phi$  and group element  $g$ ,\* Minsky and Papert define  $\phi g$  to be the predicate that, for each  $X$ , has the value  $\phi(gX)$ . Thus, one will always have  $\phi g(X) = \phi(gX)$ .  $\Phi$  will be said to be closed under  $G$  if for every  $\phi$  in  $\Phi$  and  $g$  in  $G$  the predicate  $\phi g$  is also in  $\Phi$ . If a perceptron predicate is invariant under a group,  $G$ , then its coefficients need depend only on the  $G$ -equivalence classes of their  $\phi$ 's [672].

The Group Invariance Theorem states that if:

- (i)  $G$  is a finite group of transformations of a finite space,  $R$ ;

\*Given a group  $G$ , two figures,  $M$  and  $N$ , are  $G$ -equivalent if there is a member  $g$  of  $G$  for which  $M = gN$ .



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- (ii)  $\Phi$  is a set of predicates on that space closed under  $G$ ;  
 (iii)  $\psi$  is in  $L(\Phi)$  and invariant under  $G$ . Then, there exists a linear representation of

$$\psi = \left[ \sum_{\varphi \in \Phi} \beta_{\varphi} \varphi > G \right]$$

for which the coefficients  $\beta_{\varphi}$  depend only on the  $G$ -equivalence class of  $\varphi$ , that is if  $\varphi \equiv \varphi'$  then  $\beta_{\varphi} \equiv \beta_{\varphi'}$ .

$L(\Phi)$  is the set of all predicates for which  $\psi$  is a linear threshold function with respect to  $\Phi$ , and a predicate is a function that has two possible values, i.e., a binary function.  $\psi$  is a linear threshold function with respect to  $\Phi$ , ( $\varphi$  is in  $L(\Phi)$ ), if there exists a number  $\theta$ , and a set of numbers,  $\alpha_{\varphi}$  one for each  $\varphi$  in  $\Phi$ , such that:

$$\psi(X) = \left[ \sum_{\varphi \in \Phi} \alpha_{\varphi} \varphi(X) > \theta \right]. \quad (7.54)$$

*Restrictions on Perceptron Operations and Limitations in Geometric Patterns That Can Be Recognized*

Perceptrons are not without restrictions in the types of operations that can be performed and the geometric patterns that can be recognized.

*Restrictions of Geometry.* The perceptron operations discussed by Minsky and Papert have a receptor geometry restricted as follows:

1. The number of points (or receptive elements) is limited. Hence, the predicates of the points are of limited order.
2. The distances between points are restricted. Hence, their predicates are diameter-limited.

Order has to do with the number of characteristic variables needed to represent a set of particular functions. For example, the order of  $\psi$  is the smallest number,  $K$ , for which a set  $\Phi$  of predicates can be found satisfying:

$$|S(\varphi)| \leq K \text{ for all } \varphi \text{ in } \Phi, \psi \in L(\Phi)$$

where  $S(\varphi)$  is that subset of receptors,  $r_1, r_2, \dots, r_n$ , upon which  $\psi(X)$  (the set of functions required for recognizing  $X$ ) really depends, and  $L(\Phi)$  is the linear threshold function of  $\Phi$ , the set of all predicates that can be defined by Eq. 7.54.

Linear threshold function perceptron operations are of order 1. So are all the Boolean functions of two variables except for:

- i. Exclusive-or ( $XY' + X'Y > 0$ ) and
- ii. Its complement identity,  $X \equiv Y$  ( $XY + X'Y' > 0$ )

which are of order 2.

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**Type of Processing Operations.** Perceptrons are particularly good at doing processing operations of the types called "local" or "conjunctively local" by Minsky and Papert [672]. By local is meant that all tests (analytic or logical) can be done independently and the final decision can be made by a logically simple procedure such as unanimity of all tests.

A predicate,  $\psi$ , is conjunctively local of order  $K$  if it can be computed by a set  $\Phi$  of predicates  $\varphi$  such that:

- i. Each  $\varphi$  depends on no more than  $K$  points of the space  $R$ ;
- ii.  $\psi(X) = \begin{cases} 1 & \text{if } \varphi(X) = 1 \text{ for every } \varphi \text{ in } \Phi \\ 0 & \text{otherwise.} \end{cases}$

Such processing will enable a perceptron to distinguish convex from non-convex figures at the receptors by the test that if there exist three receptor points,  $p$ ,  $q$ , and  $r$ , such that  $q$  is in the line segment joining  $p$  and  $r$ , and

$$\begin{aligned} p & \text{ is in } X, \\ q & \text{ is not in } X, \\ r & \text{ is in } X, \end{aligned}$$

then the set  $X$  is not convex (Fig. 7.28). Thus,  $\psi_{\text{convex}}(X)$  is conjunctively local of order 3 by application of this three-point rule [672].

Interestingly, the determination of connectedness between points can be shown not to be conjunctively local of any order in a diameter-limited perceptron processing operation. Hence, perceptrons of this type cannot compute connectedness of geometric figures whereas they can compute convexity. However, as inspection of Fig. 6.6C will indicate, we, too, have our difficulties in determining connectedness.

#### Types of Perceptrons

Given that "a Perceptron is a device capable of computing all predicates which are linear in some given set  $\Phi$  of partial predicates" [672], five different types of perceptrons can be distinguished. They are:

1. *Diameter-limited Perceptrons*—the set of points upon which each  $\varphi$  depends (for each  $\varphi$  in some given set  $\Phi$ ) is restricted not to exceed a certain fixed diameter in the plane.
2. *Order-restricted Perceptrons*—a perceptron has order  $\leq n$  if no member of  $\Phi$  depends on more than  $n$  points.
3. *Gamba Perceptrons*—each member of  $\Phi$  may depend on all the points but must be a linear threshold function, with each member of  $\Phi$  itself being computed by a perceptron of order 1. Thus,

$$\varphi_i = \left[ \sum_j \beta_{ij} r_j > \theta_i \right]$$

(each  $\varphi_i$  is a threshold perceptron of order 1) and

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## Determination of Convexity by Three-Point Rule

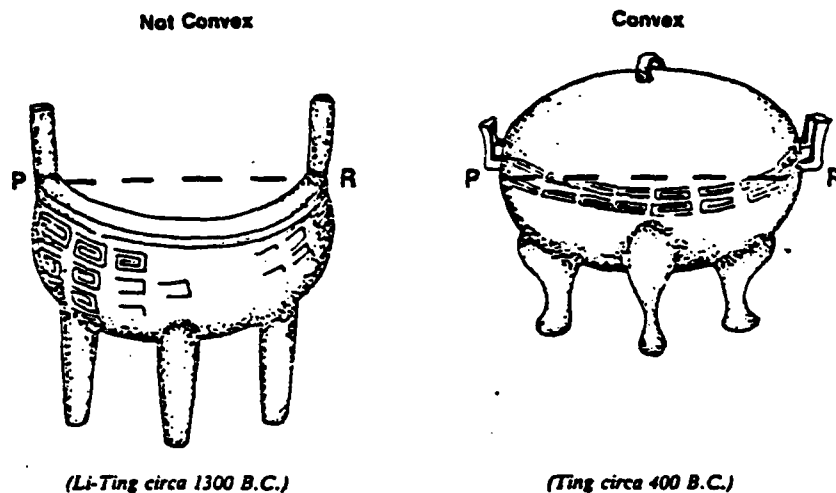


Fig. 7.28. Determination of convexity by three-point rule [672]. Draw a straight line connecting surface points such as P and R. If a third point, taken anywhere along this line, is inside the space of the object, the surface is convex.

$$\psi_{\text{gamba}} = \left\{ \sum_i \alpha_i \left[ \sum_j \beta_{ij} r_j > \theta_i \right] > \theta \right\} \quad (7.55)$$

The Gamba perceptron is thus a two-layered perceptron. Note, however, that no improvement is afforded by any multi-layered system, without loops, in which there is an order restriction at each layer wherein only predicates of finite order are computed.

4. *Random Perceptrons*—the  $\varphi$ 's are random Boolean functions. They are order-restricted and  $\Phi$  is generated by a stochastic process according to an assigned distribution function (cf. Rosenblatt [838-841]).

5. *Bounded Perceptrons*— $\Phi$  contains an infinite number of  $\varphi$ 's, but all the  $\alpha_\varphi$  lie in a finite set of numbers [672].

#### Size, Speed, and Layer-Hierarchy Considerations in Perceptron Operations

Given application of the group invariance theorem to analysis of perceptrons of the above types, several observations may be drawn concerning effects of size, speed, and layer or hierarchy of operation.

First, using more "memory" does not seem to advance the kinds or efficiencies of linear threshold operations that are performed. This is interesting because many believe that adding memory will greatly improve the types of

## Specific Theories of Line Labeled Information Handling 393

operations that can be performed. Minsky and Papert would suggest that design is more important than size.\*

Second, it should be possible to specify connection-matrices between elements that will optimize the efficiency of processing vis-à-vis the number of elements involved. Examples of different connection matrices are shown in Fig. 7.29.

*Multilayer Perceptrons with Loops*

According to Minsky and Papert, the group invariance theorem cannot be applied to multilayered perceptrons with loops.† The addition of loops thus reopens analytic questions. It remains to be seen how the addition of loops limits general theories of sensory information processing by perceptron-like automata.‡ Some analytic questions can be answered a priori. For example, the use of loops in processing will not improve the speed of computation afforded by loop-free serial processing. Other questions cannot. Thus, it is unclear whether or not loops afford the possibility of more complex analytic operations. Given finite order processing, a prerequisite for mathematical analysis, it is questionable whether loops afford any order-improvement beyond that possible with a hierarchical multilayered construction.

What loops do offer is the possibility of using the simple feedback principle for "training" or error correction. Minsky and Papert believe that the perceptron convergence theorem provides analytic proof that where such "learning, adaptation or self organization does occur, its occurrence can be thoroughly elucidated (mathematically)" [672].

**A Geometry of Sorting—Treatment of Motor Labeled Effectuation, Synthesis, and Decision Making**

Comparison of Fig. 7.30 with Fig. 3.42 will disclose how motor-labeled effectuation or decision making is implicit in the design of perceptrons.

What has not been treated explicitly in the course of analysis of perceptron operations is the geometry of sorting, i.e., an algebraic analysis of motor labeled effectuation comparable to that for sensory reception presented earlier. Three positions are possible. One is that this geometry is completely implicit in the classification algorithms described by Minsky and Papert (perhaps as a substructure of predicates). The second is that significant extensions of their algorithms and theory need to be made—perhaps by an expanded treatment of conditional probabilities and Markov processes.‡ The third position, that such

\*It is not yet clear if artificial intelligence performed by a large, specifically designed computer (capable of "logical" operation) can adequately simulate intelligence based on *unincorporated* design features. Logic may be used to approximate the needed features, but the results may be unsatisfactory and the errors difficult to detect, as in some of the phenomena illustrated in Chapter 6.

†Although it will be recalled that closed flowgraphs, consisting of loop circuits, can be solved.

‡Also, some loops can be eliminated by use of flowgraphs.

§Another class of algorithm that can compute connectedness may be required—Turing machines can compute connectedness; perceptrons cannot.

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## Connection-Matrices

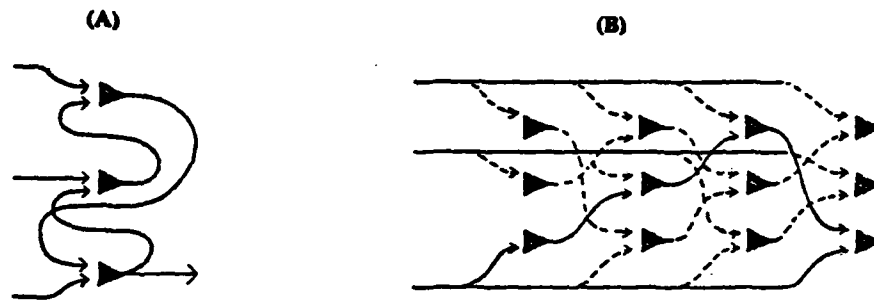


Fig. 7.29. Different connection matrices. Are those in (A) equivalent to those darkened in (B)? (There is feedback in A.) Are some elements and connections in B superfluous? (Even if different transfer functions of several elements could be combined, the connections would allow unique dependencies between inputs, elements, and outputs). (Sketches after Minsky and Papert [672].)

## A Learning Machine

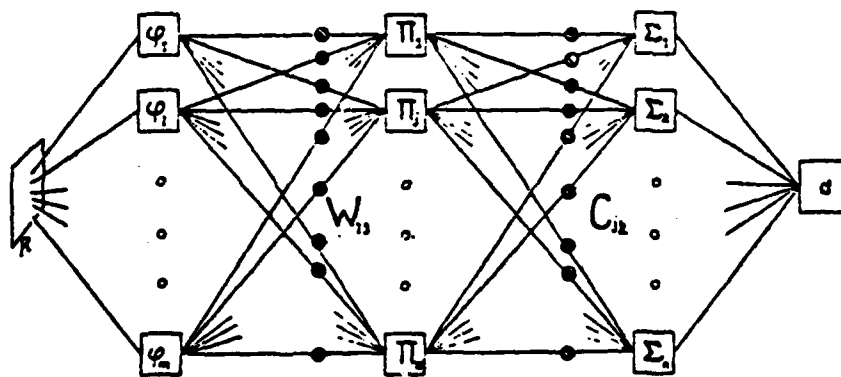


Fig. 7.30. A multilayer perceptron capable of making decisions ( $d$ ). (From Minsky and Papert [672].) The adaptations controlling  $\Delta w_{ij}$  and  $\Delta C_{jk}$  might benefit from feedback of information concerning the system state.

a geometry and analysis is unrealizable, may be dismissed if one accepts Minsky and Papert's view that workable systems are subject to analysis and this author's assertion that such systems are visible within the reflex pathways of the nervous system.

#### Classification Algorithms

The following classification algorithms for separating different sensory labeled aggregates at  $d$  in Fig. 7.30 have been suggested by Minsky and Papert [672].

1. *Perceptron convergence theorem.* Let  $F$  be a set of unit-length vectors. Let  $A \cdot \Phi$  be the vector notation of  $\sum \alpha_i \varphi_i(X)$ . If there exists a unit vector  $A^*$  and a number  $\delta > 0$  such that  $A^* \cdot \Phi > \delta$  for all  $\Phi$  in  $F$ , then a simple program (see Minsky and Papert [672], p. 167) can be devised that will converge in a finite number of iterations on a separation of all  $\Phi \in F$ . A variation of this program (see [672]) will separate more than two classes of input figures:  $F_1, F_2, \dots, F_n$ .

A limitation of this classification algorithm is that only linear separations are performed optimally by this method.

2. *Bayes' linear statistical procedure.* Again, let  $F$  be a set of unit-length vectors, with one vector,  $A_i^*$  such that  $A_i^* \cdot \Phi > \delta$  for all  $\Phi$  in  $F$ . If  $A_j = (\theta_j, \omega_{1j}, \omega_{2j}, \dots)$ ,

$$\text{where } \omega_{ij} = \text{Log} \left( \frac{P_{ij}}{1 - P_{ij}} \right)$$

and  $P$  is the probability that  $\varphi_i = 1$ , given that  $\Phi$  is in  $F_j$ , then  $\Phi \in F$  will be separated with the lowest possible error rate, given that the  $\varphi$ 's are statistically independent. (This is, remarkably, a linear formula that can perform non-linear separation.)

3. *Best planes procedure*—This is essentially an error-minimizing tracking procedure whereby the set of  $A$ 's is used for which choice of the largest  $A_i \cdot \Phi$  gives the fewest errors. The presence of false peaks in hill-climbing searches by this method may limit its applicability.

4. *Cluster analysis*—Techniques are used to minimize the least square distance between different points in the receptor array ( $R$ ) reflected by the different  $A_i \cdot \Phi$ . In effect, separation is performed on the basis of spatial clustering of each sensory aggregate. A more complete description of this approach and a cluster-analysis convergence theorem, with proof, can be found in Minsky and Papert's book [672].

5. *Exact matching or best matching*—This approach requires a large memory and is cumbersome. Each  $\Phi$  that has ever been encountered, together with the identity of its associated  $F$ -class, is stored. New inputs are "recognized" on the basis of match against the store contents. With exact matching, a tedious search results in a solution with no errors. With

\*denotes unit vector

"best" matching, a completely different type of procedure (e.g., algorithms such as those incorporating matched filtering—see Woody [1103]) is used to optimize signal detection, minimize errors, and reduce search time (see [672,704,1123]).

*Probability as a Descriptor of Motor Effectuation: The Conditional Probability of Sorting. An Algebra of Events*

Just as entropy is relatable to the uncertainty of configurations of gas molecules in a dimensional space, and provides some measure thereof, so does probability provide a measure or index of the likelihood of events. As we have seen from the work of Boltzmann and of Shannon, the events may be physical-chemical or they may be informational-probabilistic.

Just as chemical events may be described as occupying a space [328], so may other probabilistic events be described in terms of the space they occupy. The space of probabilistic events is described by set theory and Venn diagrams thereof. The sample space (Fig. 7.31) represents the number of possible different arrangements of sample points or outcomes, and each event or specific outcome in the sample space can be assigned a probability of occurrence.

Set theory is described by a set of axioms that fully define the algebra of events [cf. 240]. With respect to Fig. 7.31, they are:

1.  $A + B = B + A$  (commutative law); also for multiplication,  $AB = BA$
2.  $A + (B + C) = (A + B) + C$  (associative law); also for multiplication,  $A(BY) = (AB)Y$
3.  $A(B + C) = AB + AC$  (distributive law)
4.  $(A')' = A$  (' = "not" or the complement of whatever it follows)
5.  $(AB)' = A' + B'$
6.  $AA' = \Phi$  ( $\Phi$  = complement of  $U$ )
7.  $AU = A$  ( $U$  = union of two events—the collection of all points in either or both event spaces)

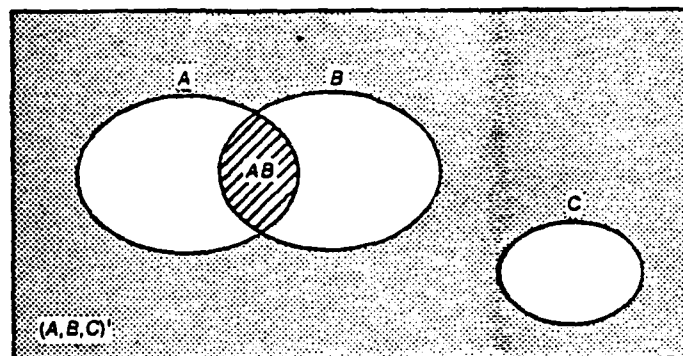
*This set of axioms is also the set of constraints by which linear systems are bound and defined.*

*Simple Probability.* Could probability be used to describe motor effectuation, i.e., the motor events (or decisional space) possible as outcomes of a particular network? If so, could some general formulation be derived, comparable to the group invariance theorem to permit a general algebraic treatment of the geometry of sorting or motor effectuation? The answer to the first question is yes; the answer to the second, perhaps. The sample space,  $S$ , of possible motor outcomes is made up of a number of points,  $E_1, E_2, \dots, E_n$ . Each point,  $E_k$ , has an expected probability of occurrence  $P(E_k)$ .\*

The probability of occurrence of event  $A$ ,  $P(A)$ , is the sum of the probabilities of all points within it. The sum of the probabilities of occurrence of all points equals 1, which is equal to the probability of the entire sample space. Thus,  $P(A)$  must be between 0 and 1.

\*Event  $A$  may be mapped from sets of  $P(E_k)$ .

Sample Space

Fig. 7.31. The sample space of  $A$ ,  $B$ ,  $C$  and  $(A, B, C)'$ .

**Conditional Probability.** Conditional probability deals with the probability of an event  $A$  occurring given that some other event  $B$  has just occurred. If the events are completely independent, the probability of event  $A$  occurring will be equal to the general probability of occurrence of event  $A$ ,  $P(A)$ . If there is some dependency, the probability of event  $A$  occurring, once  $B$  has occurred, may be different from the general probability of occurrence of event  $A$ . Bayes has systematized this relationship. If one thinks of  $B$  as the causal event and  $A$  as the affected event, the probability that  $A$  occurs given that  $B$  has occurred,  $P(A/B)$ , is equal to the general probability of occurrence of  $A$ ,  $P(A)$ , times the probability of the effect  $B$  given that the phenomenon  $A$  has occurred,  $P(B/A)$ , divided by the probability of event  $B$ ,  $P(B)$ . Thus:

$$P(A/B) = \frac{P(A) P(B/A)}{P(B)} \quad (7.56)$$

Interestingly, this theorem may be generalized to encompass the relationship of a set of events  $A_1, A_2, \dots, A_n$ . This is because  $P(B)$  will equal  $P[(A_1 + A_2 + \dots + A_n)B]$  or  $\sum P(A_i B)$ .

Thus,

$$P(B) = \sum_{i=1}^N P(A_i B) \quad (7.57)$$

It can be shown that:

$$\sum_{i=1}^N P(A_i B) = \sum_{i=1}^N P(A_i) P(B/A_i). \quad (7.58)$$

\*\*\*\*\*



2/1/76

UCLA STANDARD PROCEDURE

1110.1 - ATTACHMENT A

University of California, Los Angeles  
 Campus Veterinarian, IV-211 C.H.S.  
 Telephone: (213) 825-6240

Office Use Only

Application # 33-76C Project ID # 5-31-84-86  
 Effective 6-1-80 Expiration 5-31-84-86

## APPLICATION FOR USE OF LABORATORY ANIMAL SUBJECTS

A separate application must be completed and typewritten for each proposed project or activity utilizing animals.\* Applications should be directed to the Campus Veterinarian for review, but can be sent after funding agency deadlines. However, an approved application is required for the University to accept extramural funds and before any animals can be ordered.

Applicant Charles D. Woody, MDPhone: Office 825-0187 Home \_\_\_\_\_Department/Division NPI/MR

Title of Research or Training Project/Activity Neurophysiological Research Supporting  
the Investigation of Adaptive Network Architectures

Estimated Starting Date 6/1/80 Estimated Completion Date 5/31/84 86

The undersigned attests to the attached information, and agrees to accept responsibility that all animal use in the above-titled project or activity will be in accordance with University, Federal, and other relevant policies and regulations. Any changes will be communicated to the Chancellor's Committee/Campus Veterinarian.

Signature Charles D. Woody 5/23/80  
 Charles D. Woody, MD (Title) Professor of Anatomy and Psychiatry (Date)

\*"Animal" means any live or dead vertebrate.

For Committee Use Only

☒ Application Approved: Effective Date 6-1-80 Expiration Date 5-31-84-86 ☐ Application Disapproved

Comments:

Signature Michael Campus Veterinarian 6-2-80  
 (Title) (Date)

UCLA STANDARD PROCEDURE

2/1/76  
1110.1 - ATTACHMENT A

University of California, Los Angeles  
Campus Veterinarian, IV-211 C.H.S.  
Telephone: (213) 825-6240

Office Use Only

Application # 33-766 Project ID # 5-31-86  
Effective 6-1-80 Expiration 5-31-86

## APPLICATION FOR USE OF LABORATORY ANIMAL SUBJECTS

1. Applicant Charles D. Woody, MD Department NPI/MPR  
Phone: Office 825-0187 Home \_\_\_\_\_
2. Contact for animal problems & emergencies Charles D. Woody, MD  
Phone: Office 825-0187 Home \_\_\_\_\_
3. Title of research or training project/activity Neurophysiological Research Supporting the Investigation of Adaptive Network Architectures
4. Starting Date 6/1/80 to 5/31/84 ☐ New ☒ Continuation ☐ Renewal ☐ Supplemental
5. ☒ Extramural funding, Acad. Senate, or Cal. Inst. for Cancer Res.: Attach copy of proposal application.
6. ☐ Intramural or other funding: On cont. page outline project's objectives, animal purchasing & care budget.
7. Animal Use Sites - building(s)/room(s) 58-147, 58-159, 57-384.
8. For animals held in laboratory more than 12 hours, does housing conform to DHEW Guide: ☒ Yes ☐ No
9. Species/Strain/Breed Cat Sex \_\_\_\_\_ Age/Weight Range 20-40
10. Total number for entire project/activity per annum Expected Daily Population 12
11. ☐ Special procurement or processing needs: Specify on continuation page.
12. ☐ Procurement of dead animal material: Answer questions 1-12 only and sign application.
13. ☐ Short term use (up to 2 weeks) ☐ Long term use (more than 2 weeks) ☒ Both ☐ Breeding program
14. ☒ Standard housing, diet, sanitation & pest control ☐ Special needs: Specify on continuation page.
15. ☐ Project involves no pain or distress to animal subjects. Refer to "Guiding Principles" #5.
16. ☒ Project involves probable pain or distress to animal subjects. Details of procedures on animals presented in: ☐ proposal application ☐ continuation page ☐ attached journal reprint
17. ☒ Pain or distress relieved by anesthetic, analgesics, tranquilizers. Use cont. page for add'l drugs.  
Cite: Drug(s) NA Pentobarbital Dosage 50mg/kg Route IP
18. ☐ Pain or distress cannot be relieved. Explain basis for exception on continuation page.
19. ☐ Surgery: ☐ Nonsurvival ☒ Survival ☒ Aseptic Surgery ☐ Multiple surgeries on same animal
20. Procedure for sick/dead animals: ☐ Veterinary attention ☐ Discard ☒ Notify applicant
21. ☒ Euthanasia: Cite: drug(s) Nembutal Route IP  
Cite other method(s) \_\_\_\_\_
22. ☐ Special veterinary & technical services required: Specify on continuation page.
23. ☐ Potential biological or radiation hazard to: ☐ Humans ☐ Animals Describe on continuation page.

USE CONTINUATION PAGE(S) FOR ADDITIONAL INFORMATION